failure to provide an enabling disclosure. First, the Examiner contends that the disclosure is not enabling because "[i]t is not evident that the deposited biological materials mentioned in the claims are permanently available to the public."

Applicant encloses herewith copies of the December 13, 1991 Declaration of James F. Haley, Jr. (Exhibit A) and the June 3, 1994 Supplemental Declaration of James F. Haley, Jr. (Exhibit B). Those declarations demonstrate that applicant has converted the microorganisms referred to as G-pBR322(Pst)/HFIF3 (DSM 1791), G-pBR322(Pst)/HFIF6 (DSM 1792), and G-pBR322(Pst)/HFIF7 (DSM 1793) to deposits under the Budapest Treaty, and has averred that the deposits will be maintained for the enforceable life of the patent and that all restrictions on availability to the public will be irrevocably removed upon granting of the patent.

Microorganism G-pBR322(Pst)/HFIF1, which was not deposited, harbors a plasmid encoding the HFIF1 (IFN-B) DNA insert. As shown in Fig. 5, the HFIF1 DNA insert is a 680 base pair subset of the larger HFIF3, HFIF6 and HFIF7 DNA inserts, each of which is carried on a plasmid in one of the microorganisms deposited under the provisions of the Budapest Treaty and referred to in the declarations of James F. Haley, Jr. Because the HFIF1 insert may be derived directly from any one of the three plasmids harbored by deposited microorganisms, a G-pBR322(Pst)/HFIF1 microorganism deposit is not essential to enable one of skill in the art to produce the claimed HFIF1 DNA insert using the information disclosed in the specification as filed.

Second, the Examiner contends that the disclosure is non-enabling because it fails to teach "what amounts of human

IFN-B1 may or may not be effective in a therapeutic method of tumor treatment in humans." Applicant respectfully traverses.

First, the application as filed teaches an appropriate starting concentration range from which the skilled practitioner (i.e., physician or oncologist) can empirically determine an optimized treatment program on an individual basis. The specification states:

[i]nterferon therapy against ... tumors or cancers has been conducted at varying dosage regimes and under several modes of administration.... It is usually administered one to three times daily in dosages of 10^4 to 10^7 units.... [T]umors and cancers are usually treated by daily or multiple daily doses over several months or years. The most effective therapy for a given patient must of course be determined by the attending physician, who will consider such well known factors as the course of the disease, previous therapy and the patient's response to interferon in selecting a mode of administration and a dosage regime.

Specification, page 4, lines 11-30.

Second, several studies published before the effective filing date of this application used native human IFN-B to treat tumor cells in culture or tumors in vivo. For example, Einhorn and Strander, J. Gen. Virol., 35, pp. 573-77 (1977) (copy enclosed as Exhibit C) (referred to at specification page 5, lines 18-22), showed that purified native IFN-B inhibited osteosarcoma cell growth in vitro at concentrations of 10 and 100 units/ml (p. 574). Horoszewicz et al., Cancer Treat. Rep., 62, pp. 1899-1906 (1978) (copy enclosed as Exhibit D), showed that purified native IFN-B injected directly into human metastatic lesions (malignant melanomas of about 5 mm diameter) at a concentration of 5 x 10⁵ units (U) per day for 14 days was extremely effective in reducing tumor size and eliminating tumor cells (p. 1902). Nemoto et al., Amer. Assoc. For Cancer Res., Abs. No. 993, p. 246 (1979) (copy enclosed as Exhibit E) (referred to at specification page 6, line 35 - page 7, line 1), reported that daily injections for 30 consecutive days of 0.5 or

1.0 x 10^6 U of purified native IFN-B into subcutaneous nodules of melanoma and breast carcinoma patients (3 patients each) resulted in strong local tumor regression in all but one melanoma patient.

The relative concentrations of purified native IFN-B reported to be effective in inhibiting human tumor cell growth in publications such as those referred to above could be used in combination with applicant's disclosure by the skilled practitioner as a guide for determining an appropriate recombinant IFN-B dosage schedule for a particular tumor type in a particular patient. Accordingly, the application as filed, in view of the state of the art at the effective filing date, would have enabled one of skill in the art to initiate a therapeutic anti-tumor treatment program using the method recited in applicant's claims.

For all of these reasons, applicant respectfully requests that the Section 112, first paragraph, rejections be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner contends that claims 31 and 32 are indefinite and vague for reciting the phrase "substantially free of other proteins with which it is normally associated" in the absence of disclosure about which proteins IFN-B normally associates with. Applicant has cancelled claim 32 and has deleted the phrase "substantially free of other proteins with which it is normally associated" from amended claim 31, thus obviating this rejection.

The Examiner also objects to the phrases "characterized by" and "characterized in that," recited in claims 31 and 32, respectively. Those phrases have been deleted from

applicant's amended claims. Claim 32 has been cancelled and amended claim 31 recites "a recombinant DNA molecule comprising a DNA sequence."

Applicant's amended claims are no longer indefinite and, accordingly, applicant requests that the Section 112, second paragraph, rejections be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. \$ 103

A. The Taniguchi/Roberts/Borden Combination

The Examiner has rejected claims 31, 33 and 34 under 35 U.S.C. § 103 as "unpatentable" over Taniguchi et al., Gene, 10, pp. 11-15 (1980) ("Taniguchi") in view of Roberts, Proc.

Natl. Acad. Sci. USA, 76, pp. 5596-600 (1979) ("Roberts") and further in view of Borden et al., Annals of Internal Med., 91, pp. 472-79 (1979) ("Borden"). The Examiner contends that it would have been obvious for one of skill in the art at the time the invention was made to express the human IFN-B1 gene of Taniguchi using methods disclosed in Roberts to produce large amounts of IFN-B1 for anti-tumor therapy as suggested by Borden. Applicant traverses this rejection based on the specific facts of this case as well as the law, as described in detail below.

The success of the Examiner's rejection requires first, that the combination of <u>Taniguchi</u> and <u>Roberts</u> be proper, and second, that the combination disclose or suggest the human IFN-B polypeptide recited in applicant's amended claims.

Neither one of these requirements is met here.

1. The Combination Of Taniguchi And Roberts Is Improper

There is no basis for the Examiner's combination of

Taniguchi and Roberts. Neither document teaches or suggests the
combination: Taniguchi says nothing about expression and

Roberts says nothing about expressing an interferon, much less human IFN-8. Neither suggests resolving the difference between the prior art and the claimed invention. In re Vaeck, 947 F.2d 488 (Fed.Cir. 1991) (reversing obviousness determination because "the prior art in this case offers no suggestion, explicit or implicit, of the substitution that is the difference between the claimed invention and the prior art.")

In addition, the Examiner has presented no evidence supporting his purported combination. Ex parte Levengood, 28 USPQ2d 1300, 1301 (Bd.Pat.App.Intf. 1993) ("it is necessary for the examiner to present evidence ... that one having ordinary skill in the art would have been led to combine the relevant teachings of the applied references in the proposed manner to arrive at the claimed invention.") The only evidence here is to the opposite -- the ordinarily skilled artisan at the effective filing date of this application would not have made the Taniguchi/Roberts combination.

First, the IFN-ß gene of Taniguchi was a "copy DNA" (cDNA) on a bacterial plasmid (pBR322) unlinked to any plasmid expression control sequences. Because cDNA is enzymatically copied messenger RNA (mRNA), which starts downstream from the major expression control sequences of the gene (e.g., promoter and enhancer elements), the human IFN-ß cDNA of Taniguchi was also not linked to any endogenous expression control sequences. The Examiner does not disagree that expression or even capability for expression was missing from Taniguchi. Instead, the Examiner contends that it would have been obvious for the skilled practitioner to express Taniguchi's IFN-ß cDNA using the system of Roberts. This contention, however, is unwarranted for several reasons.

Roberts disclosed a bacterial plasmid in which the simian virus SV40 small tumor ("t") antigen gene was fused precisely to transcription and translation control sequences of the E. coli lac operon to create a "hybrid ribosome-binding site." Roberts, Abstract, lines 7-11. Bacteria transformed with such constructs were screened for SV40 expression products using antibody-containing serum from animals harboring SV40-induced tumors. SV40-related immunoreactive polypeptides were then characterized. Roberts concluded that in order to express the t antigen, a fairly precise juxtaposition between the ATG of the SV40 t gene and the lac operon Shine-Delgarno (SD) (translation control) sequences was required:

"synthesis is barely detectable if the distance between the <u>lac</u> SD sequence and the ATG of t is large (17 base pairs).... support[ing] the notion that formation of a hybrid ribosome-binding site bearing appropriately positioned SD and ATG sequences is <u>essential</u> to translation of t."

Roberts, p. 5600, Discussion, first paragraph (emphasis added).

Significantly (and a point that the Examiner ignores),

Roberts did not teach or suggest that this protocol would be
successful for expressing any other eukaryotic gene in bacteria.

In the words of Roberts, their experiment provided a "rational approach [not a solution] to the problem of obtaining expression of eukaryotic genes in bacteria." Roberts, p. 5600,

Discussion, last sentence.

Nor did <u>Roberts</u> teach or suggest that the human IFN-ß cDNA of <u>Taniguchi</u> could be fused to the <u>lac</u> operon of <u>E. coli</u>, with the same distance constraints and in the same manner as the SV40 t gene was to successfully express a human IFN-ß polypeptide in bacteria.

Roberts also did not show that the SV40 t polypeptides expressed from their <u>lac</u> fusion constructs possessed any biological activity. The t polypeptides were detected based

only on their ability to bind to SV40-specific antibodies. Thus Roberts failed to teach or suggest that their method could be used to express and isolate a biologically active, SV40 t antigen, let alone a biologically active human IFN-B, in bacteria or in any other host. Yet, applicant's claims require that the IFN-B be biologically active because otherwise it will not be useful in the claimed methods.

In addition, the <u>Roberts</u> approach could not and did not address the specific problems inherent in the expression of IFN-B. For this reason, the ordinarily skilled artisan would not have selected the <u>Roberts</u> approach in attempts to express IFN-B. Applicant submits herewith copies of the Declaration of Richard L. Cate (hereinafter referred to as "Cate Decl. ¶ __") (Exhibit F), and the Supplemental Declaration of Richard L. Cate (hereinafter referred to as "Cate Supp. Decl. ¶ __") (Exhibit G), both filed in co-pending application Serial No. 08/471,646, which describe the problems inherent in recombinantly expressing IFN-B. Cate Supp. Decl. ¶ 26.

Therefore, under the law and the facts, the Examiner's combination (even if it was proper to make, which it was not) fails to render the claimed invention unpatentable. "All the evidence on the question of obviousness must be considered." In re Piasecki, 745 F.2d 1468, 1471 (Fed.Cir. 1984). This includes the marked differences between SV40 t antigen and IFN-B. Because of these differences, there is simply no basis for selecting the Roberts approach over any other possible approach known in 1980. Cate Supp. Decl., ¶ 26.

There is also contemporaneous proof that the Taniguchi/Roberts combination is improper. None of the workers in 1980, including Dr. Ptashne, Dr. Roberts himself (who best knew the Roberts approach), and Dr. Taniguchi, used the Roberts

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approach in their attempts to express IFN-B -- they chose not to make the combination that the Examiner is making in hindsight some 15 years later. Cate Decl. ¶ 62. Instead, they used a new method (i.e., that of <u>Guarente</u>). Cate Decl. ¶ 62. Dr. Goeddel also did not use the <u>Roberts</u> approach. Cate Decl. ¶ 62.

This contemporaneous attitude towards the "Roberts approach" is powerful evidence of non-obviousness. See

Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143

(Fed.Cir. 1985). See also Ex parte Goeddel, Appeal No. 94-2099

(August 31, 1994) at 8 (copy enclosed as Exhibit H) (stating "we have attempted to place ourselves back in time" when the invention was made").

2. There Was No Reasonable Expectation Of Success

There was also no reasonable expectation of success in attempts to produce recombinant IFN- β in 1980 before applicant achieved it for the first time.

Dr. Cate's declarations detail the expected problems in the recombinant production of IFN-B and explain why these problems did not provide the ordinarily skilled artisan with a reasonable expectation of success. Cate Decl. ¶¶ 9-17, 22-35, 39-44, 46, 52, 61, 65; Cate Supp. Decl. ¶¶ 3-4. To emphasize the point, Dr. Cate expressly stated that expression of recombinant IFN-B was "unpredictable." Cate Decl. ¶ 11; Cate Supp. Decl. ¶ 4.

Applicant summarizes below why there was no reasonable expectation of success.

First, <u>Roberts</u> was a "general approach". That is insufficient. A general approach amounts only to an "obvious-to-try" situation -- a standard for obviousness that has been repeatedly rejected. <u>Gillette Co. v. S.C. Johnson & Son, Inc.</u>,

919 F.2d 720, 725 (Fed.Cir. 1990) ("An 'obvious-to-try situation' exists when a <u>general</u> disclosure may pique the scientist's interest ...").

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Further, Roberts does not solve any of the specific or general problems confronting one of skill in the art trying to express IFN-B. As described above, Roberts neither taught nor suggested that the specific sequence and distance constraints found necessary for producing SV40 t antigen polypeptides from lac-SV40 t gene fusions would be effective generally for expressing any eukaryotic gene. To the contrary, Roberts expressly acknowledges that heterologous gene expression was a "problem". See Roberts, p. 5600; Cate Decl. ¶ 54; Cate Supp. Decl. ¶ 26.

Taniguchi (as well as other prior art) identified the unique properties of IFN-\$\beta\$. Based on these properties, the ordinarily skilled artisan would have expected problems in the recombinant production of IFN-\$\beta\$. These included problems with proteolytic degradation, bioinactivity, toxicity, and insolubility. Cate Supp. Decl. \$\Pi\$ 7-8. Specific problems due to IFN-\$\beta\$'s three cysteine (Cys) residues and extreme hydrophobicity were also expected. Cate Supp. Decl. \$\Pi\$ 9-23. There was no reasonable expectation of success in overcoming those problems. Cate Supp. Decl. \$\Pi\$ 23, 27-28. See also decision of the Board of Appeals and Patent Interferences, Goeddel v. Weissmann, Interference 101,601, Paper No. 265 (December 15, 1995) ("Goeddel v. Weissmann Decision") (copy enclosed as Exhibit I) at 24-26.

Further, in 1980 the ordinarily skilled artisan could not have ruled out the possibility that IFN-B underwent post-translational processing during expression and secretion. This would have been a concern because of the discrepancy between the

molecular weight of IFN-ß as measured with the native glycosylated protein and that predicted from the sequence reported in <u>Taniguchi</u>. Cate Decl. ¶ 22. See also <u>Fantes</u>, p. 177 (Cate Supp. Decl., Exhibit 20).

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In 1980, the ordinarily skilled artisan could not have predicted that such post-translational processing would occur correctly (or at all) in a heterologous host. For this reason too, then, there was no reasonable expectation of success in attempts to produce recombinant IFN- β . This is supported by the Board in Ex parte Goeddel (supra), which stated that one skilled in the art in 1980 would not have been able to predict whether non-glycosysted IFN- β (one class of applicant's non-human interferons) would be biologically active. As a consequence, they also could not predict that such interferon could be used in the methods of claims 31 and 33-34.

Perhaps, the best evidence that on June 6, 1980, one of ordinary skill in the art would not have had a reasonable expectation of success using Roberts to express IFN-B is what the skilled workers actually did at the time. They did not use the Roberts approach. Dr. Roberts and Dr. Taniguchi did not use the Roberts approach when they collaborated to express recombinant IFN-B -- after applicant. This fact is persuasive contemporaneous evidence that those who knew the Roberts approach best did not believe that it provided a reasonable expectation of success. See Interconnect Planning, 774 F.2d at 1143 (stating "[a] retrospective view of the invention is best gleaned from those who were there at the time"). Instead, they used a new method referred to in Guarente, published after applicant's June 6, 1980 priority date. Guarente expressly states that identification of expressing transformants using the

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Roberts approach "may be laborious or impossible." Guarente, p. 544; Cate Decl. ¶ 62.

Dr. Goeddel also subsequently expressed IFN-8. He too did not use the Roberts approach. Cate Decl. \P 62.

Furthermore, Dr. Taniguchi and Dr. Roberts thought that expression of IFN-β was patentable. They filed a patent application claiming that subject matter. EP-A 0 042 246; Cate Decl. ¶ 63. So did Dr. Goeddel. EP-A 0 048 970; Cate Decl. ¶ 63. And, the Board has held Goeddel's expression of a subgenus of IFN-β -- microbially produced, mature, nonglycosylated IFN-β -- to be patentable in September 1980 -- three months after applicant expressed IFN-β the first time. See United States patent 5,460,811 ("the `811 patent") (enclosed as Exhibit J) (cited in the Supplemental Information Disclosure Statement filed concurrently herewith), which was allowed over both Roberts and Taniguchi, cited here. See also the `811 patent, p. 1, column 2, line 26 and p. 2, column 1, lines 16-17.

The foregoing demonstrates that there was no reasonable expectation of success in attempts to produce recombinant IFN-B at applicant's June 6, 1980 priority date.

The Examiner's rejection is also totally inconsistent with two recent decisions of the Board of Appeals and Patent Interferences: (1) Goeddel v. Weissmann, supra; and (2) Ex parte Goeddel, supra.

Those decisions by two different panels: (1) APJs R. Smith, Downey and W. Smith (Goeddel v. Weissmann); and (2) APJs Winters, W. Smith and Gron (Ex parte Goeddel); specifically address the same issue that underlies the Examiner's Section 103 rejection: with the DNA sequence for an interferon in hand, would it have been obvious to the skilled person to express that DNA and produce biologically active interferon in April 1980 and

in September 1980 (two months before and three months after applicant's June 6, 1980 latest priority date here).

Resoundingly, both Boards said NO. Fundamental fairness requires a consistent application of that law here.

Goeddel v. Weissmann

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This interference concerned the expression of mature IFN- α in April 1980. The Count was to the mature polypeptide itself (Decision, p.3):

"A polypeptide of about 165-166 amino acids comprising the amino acid sequence of a mature human leukocyte interferon microbially produced and unaccompanied by any corresponding presequence or portion thereof."

In April 1980, the DNA sequence encoding mature IFN- α was known and available (Decision, p. 18). In April 1980, the sequence of the mature IFN- α was also known (Decision, p. 19). This art, thus, stands in the same position and provides the same information as Taniguchi cited here by the Examiner. Roberts, the second document cited by the Examiner here, was certainly prior art in April 1980.* Yet, the Board held that the expression of the polypeptide of the Count was not enabled (Decision, pp. 24-32). See in particular, Decision, p. 24:

"As is clear from the April `80 EPO application, as of April 1980, the ability of workers to express human proteins in bacteria was a very recent advance in molecular biology, i.e., the field was in its infancy";

Decision, p. 31:

"While those individual steps and techniques may have been known at that time, in view of the embryonic nature of this field and the lack of guidance in the specification [just like in <u>Roberts</u> here], it is difficult to find a reasonable basis to conclude that one would have obtained expression of the protein by these techniques without further guidance as to the direction that experimentation should take";

^{*} A variety of prior art Goeddel documents that described expression generally and the expression mature hGH and other mature proteins stood in the place of <u>Roberts</u> in the interference (Decision, p. 21).

and Decision p. 32:

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"Boyer stated that `every protein had its own series of problems relating to expression'."

Incredibly, the Board reached its finding of non-enablement notwithstanding a fact that is <u>not</u> present here -- in April 1980, Weissmann had already expressed immature IFN- α in <u>E. coli</u> and shown that it was biologically active. This Board disregarded that fact (applicant's assignee believes improperly). It held that the expression of immature interferon was irrelevant to the issue at hand -- it was a compound outside of the Count (Decision, p. 32). How much more so is the <u>Roberts' expression of a non-interferon protein (the SV40 t antigen) irrelevant to the expression of IFN- β . On the basis of this decision alone, therefore, the Examiner should withdraw his Section 103 rejection.</u>

Ex parte Goeddel

The second Board decision -- Ex parte Goeddel -- only confirms the inappropriateness of the Examiner's Section 103 rejection here. The claim at issue in Ex parte Goeddel was a composition comprising a non-glycosylated mature human fibroblast interferon, i.e., IFN- β (Decision p. 2):

"25. A composition comprising water and a nonglycosylated polypeptide having the amino acid sequence of a mature human fibroblast interferon, said nonglycosylated polypeptide having a total of 165 or 166 amino acids and said composition being free of any glycosylated human fibroblast interferon."

The cited prior art included <u>Taniguchi</u> (cited here) and the Goeddel <u>Nature</u> article which was relied on in <u>Goeddel</u> v. <u>Weissmann</u> as showing the expression of mature hGH and other proteins (i.e., analogous to <u>Roberts</u> here). The time frame was

even later than the June 6, 1980 priority date here. The Goeddel application was filed on September 25, 1980.

Much like the rejection here, the rejection in Ex parte Goeddel was under Section 103 (Decision p. 6):

"[T]he examiner argues [in view of Taniguchi and Goeddel] that a person having ordinary skill would have been motivated to produce appellants' nonglycosylated polypeptide using recombinant expression in E. coli `because of the known benefits of such a procedure (greater yields, faster production, ability to obtain high purity)'".

The Board reversed (Decision, p. 8). It held (Decision, p. 6):

"With respect to each prior art rejection, the examiner's position presupposes that the hypothetical person having ordinary skill in this art would have reasonably expected appellants' nonglycosylated polypeptide to possess biological activity. This is not the case".

The same logic must apply here. Applicant's polypeptide is produced in a non-human host, and as such, it is not identical to known IFN- β . Its biological activity, thus, is unpredictable.

For all the reasons discussed above, the combination of <u>Taniguchi</u> and <u>Roberts</u> is both an improper one and one which had no expectation of success to those of skill in the art at the effective filing date of this invention. Accordingly, the portion of the Examiner's Section 103 rejection based on the <u>Taniguchi/Roberts/Borden</u> combination should be withdrawn.

B. The Knight/Borden Combination

The Examiner has rejected claims 32-34 under 35 U.S.C. § 103 as "unpatentable" over Knight et al., <u>Science</u>, 207, pp. 525-26 (1980) ("Knight"), in view of Borden et al., <u>Annals of Internal Med.</u>, 91, pp. 472-79 (1979) ("Borden"). The Examiner contends that it would have been obvious for one of skill in the

art at the time the invention was made to isolate human IFN-B1 in the manner of Knight and to use it for anti-tumor therapy as suggested by Borden. Applicant has obviated this rejection by cancelling claim 32. Amended claims 33 and 34 depend only from amended claim 31.

For these reasons, the amended claims are not obvious over the cited art. Accordingly, applicant requests that the Examiner withdraw the 103 rejections.

CONCLUSION

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For all of the above reasons, reconsideration and allowance of the pending claims is requested.

Respectfully submitted,

James F. Haley, Jr. (Reg. No. 27,794)

Leslie A. McDonell (Reg. No. 34,872)

Attorneys for Applicant

Barbara A. Ruskin (Reg. No. 39,350)

Agent for Applicant c/o FISH & NEAVE

1251 Avenue of the Americas New York, New York 10020-1104 Tel.: (212) 596-9000

Hereby Certify that this Correspondence is being Correspondent the U.S. Deposited with the U.S.

Examiner : J. Martinell

Group : 1805

Applicant: Walter C. Fiers

Serial No.: 387,503

Filed : July 28, 1989

FOR : DNA SEQUENCES, RECOMBINANT DNA MOLECULES AND

PROCESSES FOR PRODUCING HUMAN FIBROBLAST

INTERFERON-LIKE POLYPEPTIDES

New York, New York December 13, 1991

Hon. Commissioner of Patents and Trademarks Washington, D.C. 20231

DECLARATION OF JAMES F. HALEY, JR.

I, JAMES F. HALEY, JR., declare that:

- 1. I am the attorney of record in the aboveidentified ratent application. I make this declaration to
 set forth the facts related to the deposit of microorganisms
 referred to on pages 94-95 of that application and to the
 permanence, availability and replacement of those cultures.
- 2. I identify the following documents that demonstrate the deposit of those microorganisms and the permanence, availability and replacement of those cultures:

Exhibit 1 -- True copies of seven Deutsche

Sammlung von Mikroorganismen "Acknowledgement of Receipt and

Acceptance" for cultures HFIF-A through HFIF-G (DSM 1791
1793 and 1851-1854). The acknowledgments confirm that these
deposits were made on April 2, 1980 and June 5, 1980,

respectively, under Title 37, Code of Federal Regulations,

and the other applicable rules and regulations of the United

States Patent and Trademark Office.

Exhibit 2 -- True copies of a February 27, 1981 letter to me from the American Type Culture Collection and

(2000)

States Patent and Trademark Office.

Exhibit 3 -- True copies of an October 16, 1991

letter from me to the Deutsche Sammlung von Mikroorganismen
with enclosures including seven Deutsche Sammlung von
Mikroorganismen applications to convert into a deposit under
the Budapest Treaty the deposit of a microorganism already
deposited outside the Budapest Treaty for cultures HFIF-A
through HFIF-G (DSM 1791-1793 and 1851-1854).

Exhibit 4 -- True copies of a October 16, 1991 letter from me from the American Type Culture Collection with enclosures including two requests to convert a deposit to meet the requirements of the Budapest Treaty for the cultures HFIF-H and HFIF-I (ATCC 31824 and 31825).

Exhibit 5 -- A true copy of a Budapest Treaty

Receipt Of Request And Viability Statement from ATCC

confirming that the deposits for cultures HFIF-H and HFIF-I

(ATCC 31824 and 31825) have been converted to Budapest treaty deposits.

Exhibit 6 -- True copies of Budapest Treaty

Receipt Of Request And Viability Statements from Deutsche

Sammlung von Mikroorganismen confirming that the deposits

for cultures HFIF-A through HFIF-G (DSM 1791-1793 and 1851
1854) have been converted to Budapest treaty deposits.

axhibits, I am informed and believe that the deposits of microorganisms referred to on pages 94-95 of the above-identified application were made, have been converted to deposits under the Budapest Treaty On The International Recognition Of The Deposit Of Microorganisms For The Purposes Of Patent Procedure and are being maintained under the applicable rules and regulations of that Treaty and of

agrees to maintain the permanence of these deposits for the full enforceable term of any patent issuing from this application and to irrevocably remove all restrictions on the availability to the public of the material so deposited upon the granting of a patent in accordance with the requirements of 37 C.F.R. §§ 1.806 and 1.808.

5. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent iss. Ing thereon.

JAMES F. HALEY, JR

Signed at New York, New York this 13'th day of December, 1991.

I Hereby certify that this correspondence is being deposited with the U. S. Postal Service as First Class Mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on

Name of Person Signing

Signature of Person Signing

The microorganism mentioned be organismen.	elow has been deposited with the Deutsche Sammlung von Mikro-
Name and address of depositor:	Biogen N.V. 24 Handelskad Willemsted Curacao, Netherland Antilles
Identification reference of	curacao, Netherrand Antifres
the microorganism used by	.HFIF-A
the depositor:	HB101(G-pBR322(Pst)/HFIF 3)
Taxonomic designation of the microorganism provi- ded by the depositor:	Escherichia coli
DSM accession number of the microorganism;	DSM 1791
Date of receipt of the viable microorganism:	April 2, 1980
In addition to the identification with the provided a second seco	on reference and the taxonomic designation the depositor has cientific description of the microorganism.
X The microorganism has been	sent to the DSM directly by the depositor.
The microorganism has been	sent to the DSM on behalf of the depositor by the following nation and accession number given:
As stated by the depositor the munder the following conditions: without any restrictions	nicrooganism may be rendered accessible to any third party
according to Rule 28 EPC an	d to the agreement between the European Patent Organisation al EPO <u>5</u> , 301–307, 1978) and/or
according to the Swedish par	tent legislation and to the agreement between the Swedish Svensk Patenttidning nr 12, 1979)
in accordance with the "Dec. DSM and the German Patent O	laration of Release" to be filed by the depositor with the ffice (at present Form P 2570)
America and b) without any	37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) Code, section 122 (35 U.S.C. 122) of the United States of restriction on availability to the public of the culture tates patent wherein the deposited microorganism is part vention
X in accordance with the French	
	itions as specified by the depositor on enclosed separate
Göttingen, April 2, 19	
Place date Deu	TECHE SAMMLUNG VON MIKROORGANISHEN
	der 319 lature Gesellschaft für Biotechnologische Forschung mbH

D-3400 Göttingen

Gesellschaft für Biolechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel: (05.31) 70.08—1, Telex: 9—5.26.67

Vorsitzender des Aufsichtsrats: M.n. Dir. Dr. Friedrich Bischoff

Geschäftsführer: Dr. Maria Regina Kula Dr. Heimut Zeitträger

Bankkonto

Gebr Löbbecke, Brium, harris Konto 23 761 (BLZ 270 5-5.4)

Registergericht: Amtsgericht Braunschweig HRB 477

The microoryzmism mentioned below has bee organismen.	n deposited with the Deutsche Sammlung von Mikro-
Name and address of depositor:	Biogen N.V. 24 Handelskad Willemsted Curacao, Netherland Antilles
Identification reference of the microorganism used by the depositor:	HFIF-B HB101(G-pBR322(Pst)/HFIF 6)
Taxonomic designation of the microorganism provided by the depositor:	Escherichia coli
DSM accession number of the microorganism;	DSM 1792
Date of receipt of the viable microorganism:	April 2, 1980
In addition to the identification reference XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	e and the taxonomic designation the depositorX Ya X escription of the microorganism.
X The microorganism has been sent to the	DSM directly by the depositor.
	DSM on behalf of the depositor by the following
As stated by the depositor the microoganism under the following conditions:	may be rendered accessible to any third party
without any restrictions	
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ush and the German Patent Uffice (at p	
America and b) without any restriction	f Federal Regulations, section 1.14 (37.CFR 1.14) ion 122 (35 U.S.C. 122) of the United States of on availability to the public of the culture t wherein the deposited microorganism is part
X in accordance with the French patent 1	
in accordance with the conditions as spacet.	pecified by the depositor on enclosed separate
Göttingen, April 2, 1980	,
Place date DEUTSCHE SAMM	LUNG VON MIKROORGANISMEN
Gesellechaft für i	der Signature Biotechnologische Forschung mbH Grisebachstraße 8 -3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.; (05.31) 70.08—1, Telex: 9—5.26.67

Vorsitzender des Aufsichtsrats: Min, Dir. Dr. Friedrich Bischoff

Geschäftsführer: Dr. Maria Regina Kula Dr. Helmut Zeitträger

Bankkonto:

Gebr. Löbbecke, Braunschweig Konto 23 781 (BLZ 270 305 00)

Registergericht: Amtsgericht Braunschweig HRB 477

The microorganism mentioned below he organismen.	as been deposited with the Deutsche Sammlung von Mikro-
Name and address of depositor:	Biogen N.V. 24 Handelskad Willemsted Curacao, Netherland Antilles
Identification reference of the microorganism used by the depositor:	HFIF-C HB101(G-pBR322(Pst)/HFIF 7)
Taxonomic designation of the microorganism provided by the depositor:	Escherichia coli
DSM accession number of the microorganism;	DSM 1793
Date of receipt of the viable microorganism:	April 2, 1980
In addition to the identification ref	erence and the taxonomic designation the depositor has fic description of the microorganism.
X The microorganism has been sent	to the DSM directly by the depositor.
The microorganism has been sent (depository under the designation	to the DSM on behalf of the depositor by the following and accession number given:
As stated by the depositor the microogunder the following conditions:	ganism may be rendered accessible to any third party
without any restrictions	
and the USM (Official Journal EPO	
Patent Uffice and the DSM (Svensk	
Don and the German Patent Office	
America and b) without any restri	ode of Federal Regulations, section 1.14 (37.CFR 1.14) section 122 (35 U.S.C. 122) of the United States of ction on availability to the public of the culture patent wherein the deposited microorganism is part n
X in accordance with the French pate	ent law
in accordance with the conditions sheet.	as specified by the depositor on enclosed separate
Göttingen, April 2, 1980	· · · · · · · · · · · · · · · · · · ·
	CHE SAMMLUNG VON MIKROORGANESMENITE
Ges	elischaft für Biotechnologische Forschung mbH Grisebachstraße 8

003-D979

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05.31) 70.08—1, Telex: 9—5.26.67

Vorsitzender des Aufsichtsrats; Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer: Dr. Mana-Regina Kuta Dr. Helmut Zeitträger

Bankkonto: Gebr. Löbbecke, Braunschweig Konto 23 781 (BLZ 270 305 00) Registergericht: Amtsgericht Braunschweig HRB 477

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikro-

eccording to the Swedish patent leg Patent Office and the DSM (Svensk P in accordance with the "Declaration DSM and the German Patent Office (a in accordance with a) Title 37, Cod and Title 35, United States Code, s America and b) without any restrict upon granting of a United States pa of the disclosure of the invention in accordance with the French paten in accordance with the conditions a sheet. Göttingen, June 5, 1980	pislation and to the agreement between the Swedish atenttidning nr 12, 1979) of Release" to be filed by the depositor with the it present Form P 2570) be of Federal Regulations, section 1.14 (37.CFR 1.14) ection 122 (35 U.S.C. 122) of the United States of ion on availability to the public of the culture tent wherein the deposited microorganism is part
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and the DSM (Official Journal EPO 5 eccording to the Swedish patent leg Patent Office and the DSM (Svensk P in accordance with the "Declaration DSM and the German Patent Office (a in accordance with a) Title 37, Cod and Title 35, United States Code, s America and b) without any restrict upon granting of a United States pa of the disclosure of the invention in accordance with the French paten	pislation and to the agreement between the Swedish atenttidning nr 12, 1979) of Release" to be filed by the depositor with the present Form P 2570) le of Federal Regulations, section 1.14 (37.CFR 1.14) ection 122 (35 U.S.C. 122) of the United States of ion on availability to the public of the culture tent wherein the deposited microorganism is part
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eccording to the Swedish patent leg Patent Office and the DSM (Svensk P in accordance with the "Declaration DSM and the German Patent Office (a	rislation and to the agreement between the Swedish Patenttidning nr 12, 1979) of Release to be filed by the depositor with the present Form P 2570)
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acroading to Rule 28 EPC and to the	agreement between the European Patent Organisation
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s stated by the depositor the microogar nder the following conditions:	nism may be rendered accessible to any third party
depository under the designation as	nd accession number given:
	the DSM directly by the depositor. the DSM on behalf of the depositor by the following
የዕዚነወዚዊ / has not provided a scientifi ግ	_
ate of receipt of the iable microorganism:	June 5, 1980
OSM accession number of the microorganism;	DSM 1851
Taxonomic designation of the microorganism provi- ded by the depositor:	Escherichia coli
Identification reference of the microorganism used by the depositor:	HFIF-D M5219 (G-pPLa-HFIF-67-12)
Name and address of depositor:	BIOGEN N.V. 24 Handelskad Willemsted, Curacao, Netherland Antilles

Vorsitzender des Aufsichtsrats: Min. Dir. Dr. Friedrich Bischoff

Geschättsführer: Dr. Maria-Regina Kula Dr. Helmut Zeitträger

Bankkonte: Gebr. Löbbecke, Braunschweig Konto 23 781 (BLZ 270 305 00)

Registergericht: Amtsgericht Braunschw HRB 477

The microorganism mentioned below borganismen.	has been deposited with the Deutsche Sammlung von Mikro-
Name and address of depositor:	BIOGEN N.V. 24 Handelskad Willemsted, Curacao, Netherland Antilles
Identification reference of the microorganism used by the depositor:	HFIF-E K12aHI (G-pPLa-HFIF-67-12)
Taxonomic designation of the microorganism provi- ded by the depositor:	Escherichia coli
DSM accession number of the microorganism;	DSM 1852
Date of receipt of the viable microorganism:	June 5, 1980
CO	ference and the taxonomic designation the depositor \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\
X The microorganism has been sent	to the DSM directly by the depositor.
The microorganism has been sent depository under the designation	to the DSM on behalf of the depositor by the following and accession number given:
	ganism may be rendered accessible to any third party
uithout any rustrictions	
The Die Par (DITTELET SOUTHER CI	the agreement between the European Patent Organisation 0 5, 301-307, 1978) and/or
- Totalit Office Bild the Dall (Svens	legislation and to the agreement between the Svedish k Patenttidning nr 12, 1979)
Colimbi - Geene Of 12ce	ion of Release" to be filed by the depositor with the (at present Form P 2570)
America and b) without any restriction upon granting of a United States of the disclosure of the invention	
X in accordance with the French pat	
in accordance with the conditions sheet.	s as specified by the depositor on enclosed separate
Göttingen, June 5,1980	~ Chi
lace date	SAMMLUNG VON MIKROORGANISMEN
Cate	der Signature chaft für Biotechnologische Forschung mbH
	Grisebachairate e D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05.31) 70.08—1, Telex: 9—5.28.67

Vorsitzender des Aufsichtsrats:

Min, Dir. Dr. Friedrich Bischoff

Geschäftsführer: Dr. Marra-Regina Kula Dr. Helmut Zeitträger

Bankkonto; Gebr. Löbbecke, Braunschweig Konto 23 781 (BLZ 270 305 00)

Registergericht: Amtsgericht Braunechweig HRB 477

V17-CUU

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikro-organismen.

Name and address of depositor:

BICGEN N.V. 24 Handelskad Willemsted,

Curacao, Nétherland Antilles

Identification reference of the microorganism used by the depositor:

HFIF-F

M5219 (G-pPLa -HFIF-67-12419)

Taxonomic designation of the microorganism provided by the depositor:

Escherichia coli

DSM accession number of the microorganism:

DSM 1853

Date of receipt of the viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositorXHAX provided / has not provided a scientific description of the microorganism.

- $oldsymbol{ol}}}}}}}}}}}}}}}}}}}}}}}}}$
- O The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microoganism may be rendered accessible to any third party under the following conditions:

- O without any restrictions
- $\[igoplus \]$ according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO $\underline{5}$, 301-307, 1978) and/or
- according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
- \bigcirc in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
- in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR I.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
- in accordance with the French patent law
- $\dot{\text{O}}$ in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5,1980

D. Obur

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMISMINITE

Gesellschaft für Biotechnologische Forschung mbH Grisebachetraße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05.31) 70.08—1, Telex: 9—5.26.67

Vorsitzender des Aufsichtsrats: Min. Dir. Dr. Friedrich Bischoff Geschäftsführer: Dr. Maria-Regina Kula Dr. Helmut Zeitträger Bankkonto: Gebr. Löbbecke, Braunschweig Konto 23 781 (BLZ 270 305 00)

Registergericht: Amtagericht Braunschweig HRB 477

03-0979

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address of depositor:

BIOGEN N.V. 24 Handelskad Willemsted,

Curacao, Netherland Antilles

Identification reference of the microorganism used by

the depositor:

HFIF-G

M5219 (G-pPlc-HFIF-67-8)

Taxonomic designation of the microorganism provided by the depositor:

Escherichia coli

DSM accession number of

the microorganism:

DSM 1854

Date of receipt of the viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositorXHMA 於於於於人 / has not provided a scientific description of the microorganism.

- igotimes The microorganism has been sent to the DSM directly by the depositor.
- The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microoganism may be rendered accessible to any third party under the following conditions:

- O without any restrictions
- according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
- according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
- in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)
- in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part
- of the disclosure of the invention in accordance with the French patent law
- in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5,1980

DEUTSCHE SAMMLLING VON MIKROORGANISMI

Place

date

der Signature

Gesellschaft für Biotechnologische Forschung mbH Grisebachstraße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05.31) 70.08—1, Telex: 9—5.26.67

Vorsitzender des Aufsichtsrats: Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer: Dr. Maria-Regina Kula Dr. Helmut Zeitträger

Gebr. Lobbooke, Braunschweig Konto 23 781 (BLZ 270 305 00) Registergericht: Amtsgaright Diamschweig HRB 477

AMERICAN TYPE CULTURE COLLECTION

12301 PARKLAWN DRIVE ROCKVILLE, MARYLAND 20852

February 27, 1981

James F. Haley, Jr., Esq. Attorney for Biogen N.V. c/o Fish & Neave 277 Park Avenue New York, New York 10172

Gentlemen:

We received on February 26, 1981 a deposit of cultures of organisms identified as Escherichia coli M5219(G-pPLa-HFIF-67-12/MI), HFIF-H, and Escherichia coli HBI01(p 1325)-qHFIF-4), HFIF-I.

These strains have been assigned the ATCC numbers 31824 and 31825, respectively.

We understand that these organisms are being deposited in the American Type Culture Collection (ATCC) in connection with the filing of an application for a patent.

We further understand that the deposit of these cultures does not grant to ATCC during the effective term of the patent anticipated a license, either expressed or implied to infringe the patent, and our release of these cultures to others does not grant them a license, either expressed or implied, to infringe the patent.

We further understand that if these cultures should die or be destroyed during the effective life of the patent it shall be your responsibility to replace them with living cultures of the same organisms.

We agree in consideration for a one-time service charge, not to distribute these cultures or any information relating thereto or to their deposits until such time as a patent has been issued disclosing the above deposits except in accordance with a U.S. Patent Office Rule of Practice, Rule 14, or until you authorize us to make these strains available. After a patent is issued and we are so informed the cultures will be made available for distribution to the public. The ATCC agrees to maintain the cultures for a period of 30 years from the deposit date. Non-payment of the service charge within 90 days of the deposit date relieves the ATCC from the above provisions.

Payment in the amount of \$1,140.00 received. Thank you.

Sincerely yours.

By: (Mrs.) Bobbie A. Brandon

An independent non-profit organization incorporated in Washington, D. C. and devoted to the preservation of reference cultures and their distribution to the scientific community.

1.		<u> </u>	PTA-HFTF-67-12AMT)	Do not urite in this box
2.	Strain designations other than	ATCC number	HFIF•H	Mac 1 3/8211-
3.	Is this the type strain of this			Accession date 2/26/31
4 .	If this strain has been designa strain, please cite reference	ted in the liters	ture as the type	Date received 2/36/8
5. _.	Hame and address of depositor:	15 Pieterma	aai etherlands Antil	.les
•	Isolated by			
	from	a	ate	·
	If you did not isolate this stre	sin, indicate from	whom you received it:	
•			,	
	ATCC - depositor -	~	-	
•	Reason for deposit:	•	• •	•
•	Requested by ATCC	Subspecies		, · ·
	Produces the antibiotic		Assay of	•
				Patent
	Production of		Other _	
	••			
•	Maintenance: Medium (attach formula) LB	Broth or ba	ctotryptone	
•	Haintenance: Medium (attach formula) LB Temperature 28°C	Broth or ba	ctotryptone	d with 50 مرg/ml Kanam
•	a) Does this organism survive: b) Recommended method for long-t Freeze drying or LB	Broth or ba Other LB Br Freeze drying! era preservation: Broth/glyce	ctotryptone coth supplemente Yes Freezing!	Yes (poorly) -80°C
•	Temperature 28°C a) Does this organism survive: b) Reconsended method for long-t Freeze drying or LB Is this strain zoopathogenic?	Broth or ba Other LB Br Freeze drying? era preservation: Broth/glyce No If so, would (see rever	ctotryptone coth supplemente Yes Freezing! crol or DMSO at d you classify it as class side for description	Yes (poorly) -80°C ass 2, 3, or %? of classes)
•	Temperature 28°C a) Does this organism survive: b) Recommended method for long-t Freeze drying or LB Is this strain zoopathogenic? Is this strain phytopathogenic? If so, a) Is the geographical b) Would you recommend investigator regardl	Broth or ba Other LB Br Freeze drying? era preservation: Broth/glyce NO If so, would (see rever) NO (Information of the this strain the strain the seas of his location of the season of his location of his location of the season of his location	roth supplemente Yes Freezing! erol or DMSO at d you classify it as classe side for description a required by Plant Quarties organism general, life made available to any	Yes (poorly) -80°C ass 2, 3, or %? of classes) entine Division, USDA) mited, or unknown (encircle)? equalified
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•	Temperature 28°C a) Does this organism survive: b) Recommended method for long-t Freeze drying or LB Is this strain zoopathogenic? Is this strain phytopathogenic? If so, a) Is the geographical b) Would you recommend investigator regardl c) If not, what limits Please attach a complete descrip	Broth or ba Other LB Br Freeze drying? era preservation: Broth/glyce NO If so, would (see rever) NO (Information of the this strain the strain the strain the strain the strain the strain that this strain the strain that the strain t	roth supplemente Yes Freezing? Prol or DMSO at Id you classify it as classe side for description In required by Plant Quarties organism general, life made available to any the distribution of the control of the distribution is	Yes (poorly) -80°C ass 2, 3, or %? of classes) entine Division, USDA) mited, or unknown (encircle)? qualified is strain? given in accompanying
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•	Temperature 28 °C a) Does this organism survive: b) Recommended method for long-t Freeze drying or LB Is this strain zoopathogenic? Is this strain phytopathogenic? If so, a) Is the geographical b) Would you recommend investigator regardl c) If not, what limits Please attach a complete descrip reprint. References (Please enclose two (Broth or ba Other LB Br Freeze drying? era preservation: Broth/glyce NO If so, would (see rever) NO (Information of the this strain the strain the strain the strain the strain the strain that this strain the strain that the strain t	roth supplemente Yes Freezing? Prol or DMSO at Id you classify it as classe side for description In required by Plant Quarties organism general, life made available to any the distribution of the control of the distribution is	Yes (poorly) -80°C ass 2, 3, or %? of classes) entine Division, USDA) mited, or unknown (encircle)? qualified is strain? given in accompanying
•	a) Does this organism survive: b) Recommended method for long-t Freeze drying or LB Is this strain zoopathogenic? If so, a) Is the geographical b) Would you recommend investigator regardl c) If not, what limits Please attach a complete descrip	Broth or ba Other LB Br Freeze drying? era preservation: Broth/glyce NO If so, would (see rever) NO (Information of the this strain the strain the strain the strain the strain the strain that this strain the strain that the strain t	roth supplemente Yes Freezing? Prol or DMSO at Id you classify it as classe side for description In required by Plant Quarties organism general, life made available to any the distribution of the control of the distribution is	Yes (poorly) -80°C ass 2, 3, or %? of classes) entine Division, USDA) mited, or unknown (encircle)? qualified is strain? given in accompanying
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	Temperature 28 °C a) Does this organism survive: b) Recommended method for long-t Freeze drying or LB Is this strain zoopathogenic? Is this strain phytopathogenic? If so, a) Is the geographical b) Yould you recommend investigator regardl c) If not, what limits Please attach a complete descrip reprint. References (Please enclose two (Broth or ba Other LB Br Freeze drying? era preservation: Broth/glyce NO If so, would (see rever) distribution of the this strain the strain the strain the strain that this strain that the strain tha	retotryptone Toth supplemente Yes Freezing? Prol or DMSO at Id you classify it as clarse side for description In required by Plant Quarties organism general, lifted any and available to any at the distribution of the sin unless description is Ent reprint, if available Signt reprint, if available	Yes (poorly) -80°C ass 2, 3, or %? of classes) entine Division, USDA) mited, or unknown (encircle)? qualified is strain? given in accompanying

COLLECTION OF BACTERIA

1.	Scientific name of organism E. Coli HB101 (D[325] - GHFIF-4) Do not write in this box
2.	Strain designations other than ATCC number HFIF-I ATCC # 3/825
	Is this the type strain of this organism (see reverse side)? NO Accession date 2/26/3
	If this strain has been designated in the literature as the type strain, please cite reference:
5.	Name and address of depositor: Biogen N.V. 15 Pietermaai Curacao, Netherlands Antilles
6.	Isolated by
	from date
7.	If you did not isolate this strain, indicate from whom you received it:
	ATCC depositor
8.	Reason for deposit: Requested by ATCC Subspecies Subspecies
	Produces the antibiotic Assay of
	Production of Patent Other Patent
9.	Maintenance: Medium (attach formula) LB Broth or bactotryptone
	Temperature Other LB Broth supplemented with 100 mg/ml carbenic
10.	a) Does this organism survive: Freeze drying? Yes Freezing: Yes (poorly) b) Recommended method for long-term preservation: Freeze drying or LB Broth/glycerol or DMSO at -80°C
11.	Is this strain zoopathogenic: NO If so, would you classify it as class 2, 3, or 4:
12.	Is this strain phytopathogenic: NO (Information required by Plant Quarantine Division, USDA) If so, a) Is the geographical distribution of this organism general, limited, or unknown (encircle): b) Would you recommend that this strain be made available to any qualified investigator regardless of his location:
	e) If not, what limits would you place on the distribution of this strain?
13.	Please attach a complete description of this strain unless description is given in accompanying reprint.
14.	References (Please enclose two (2) of each pertinent reprint, if available):
15.	Comments:
	Ja J. Haly Je
ATCE	Form 1-B (1971) Attorney for Biogen N.V.

ROSERT C. MORGAN KENNETH B. MERMAN EOWARD F. MULLOWNEY ROSERT R. JACKSON JESSE J. JENNER W EDWARD BAILEY PATRICIA A. MARTONE

KEVIN J. CULLIGAN GLENN A. OUSTERHOUT SUSAN PROGOFF MARGARET A. PIERRI PON E. SHULMAN DOUGLAS J. DILBERT DENISE L. LORING JEFFREY H INGERHAN

October 16, 1991

TELECOPIER: (2(2) 7(5-0674

FREDERICK P FISH 1855-1930 CHARLES NEAVE 1867-1937

> Mrs. Bobbie Brandon American Type Culture Collection 12301 Parklawn Drive Rockville, MD 20852

DAVIDC. PLACHE JANE A. MASSARO DUANE-DAVID HOUDH MITCHELL P. BROOK JOHN F. WAND
EOWARD J DEFRANCO
MARK O ROWLAND
PHILIPPEY RIESEN
MARK O. ENGELMANN
ERIC R MUSSARD
DAVID A LOEWENSTEIN
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JOHN H HINTZ
JOHN R STORELLA
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JOHN M. DESMARAIS
LOCKIS YEENKERS
LESLIE A. MCDONELL
CHRISTOPHER P DODZIELA EDWARD J DEFRANCO

NICOLA PISANO
DONALD K REEDV
GASRIELLE E HIDDINS
JENNIFER M MALL
DONALD L RHOADS
ELIZABETH M ALORIDOE ELIZABETH M ALORIDOE
CLAYS WILSON
SRENDAJ PANICHI
JEREMYLACK
EVANM GSELL
JAMES P SERGIN
ROMALDA KRASNOW
JEFFREYN HERSH
LIANNAC KALMAR
BRADOTOD FRIEDHAN
DEBRAA SONTEMPO
LORETTAA MIRAGLIA
MOREYS WILDOES
CHRISTOPHER J HARNET
MARIE H MACNICHOL
WILLIAMA SCHONEMAN HARNETT

Biogen - B8/B8 CIP Deposits identified as ATCC 31824 and ATCC 31825

Dear Mrs. Brandon:

We have enclosed two (2) requests for conversion of the above-identified deposits to meet the requirements of the Budapest Treaty. The ATCC designations, as well as the strain designations given by the depositor, are identified on the request forms. In addition, we enclose copies of the letter of receipt of these deposits and of the original deposit applications containing the media and culture requirements.

Please note that the original depositor has undergone a corporate name and address change, from Biogen N.V., 15 Pietermaai, Curacao, Netherlands Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hestiate to contact us.

Thanks for your help.

Yours very truly,

Jamés F. Haley,

Ivor R. Elrifi

Attorneys for Biogen, Inc.

JFH/IRE:bb Enclosures

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

	B101 (p[325]-qHFIF-4)
2. Strai	n designation given by the depositor (number, symbols, etc.)
	s an original deposit under the Budapest Treaty?
4. Is thi	s a request for a conversion of a deposit already at the ATCC to meet the requirements of the Budapest y? (If so, indicate ATCC designation.) Yes, ATCC 31825
	deposit a mixture of microorganisms or cells?
6. Detail	s and conditions necessary for the cultivation of the strain, for its storage and for testing its viability and where a mixture of microorganisms is deposited, descriptions of the components of the mixture and at least the methods permitting the checking of their presence. See attached sheets
	ication of the properties of the strain which are or may be dangerous to health or the environment, or an ion that the depositor is not aware of such properties. Depositor is not aware of any
510	perties of the strain which are or may be dangerous to health or
the	environment.
	ommended that sufficient description be provided to allow the ATCC to confirm that the strain deposited by conforms to that which the depositor states is being deposited (i.e., Gram negative rod).
b. Fo	or cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics so list the antibiotics) or hybridoma deposits please complete. What is the isotype of antibody produced?
b. Fo	r cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics so list the antibiotics) r hybridoma deposits please complete. What is the isotype of antibody produced? rain zoopathogenic? No phytopathogenic? No
b. Fo Is this st Does thi If so, wh Guidelin	r cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics so list the antibiotics) r hybridoma deposits please complete. What is the isotype of antibody produced? rain zoopathogenic? No phytopathogenic? No sis strain contain plasmids relevant to the patent process? at physical containment level is required for experiments as described in the National Institutes of Health es involving Recombinant DNA Molecules (i.e., P1, P2, P3 and P4 facility)?
b. Fo Is this st Does thi If so, wh Guidelin	r cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics so list the antibiotics) r hybridoma deposits please complete. What is the isotype of antibody produced? rain zoopathogenic? No phytopathogenic? No s strain contain plasmids relevant to the patent process?
b. For Is this st Does this If so, whe Guideling	r cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics so list the antibiotics) r hybridoma deposits please complete. What is the isotype of antibody produced? rain zoopathogenic? No phytopathogenic? No sis strain contain plasmids relevant to the patent process? last physical containment level is required for experiments as described in the National Institutes of Health les involving Recombinant DNA Molecules (i.e., P1, P2, P3 and P4 facility)?
b. For Is this st Does this If so, whe Guideling	recell culture deposits please complete. Is the cell being cultured in the presence of antibiotics so list the antibiotics. In hybridoma deposits please complete. What is the isotype of antibody produced? In phytopathogenic? In phytopath
b. For Is this st Does this If so, whe Guideling	r cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics so list the antibiotics) r hybridoma deposits please complete. What is the isotype of antibody produced? rain zoopathogenic? No phytopathogenic? Yes sat physical contain plasmids relevant to the patent process? nat physical containment level is required for experiments as described in the National Institutes of Health less involving Recombinant DNA Molecules (i.e., P1, P2, P3 and P4 facility)? The process of these questions are recommended but not required. FOR ATCC USE ONLY

Form BP/1 (Page 1 of 2)

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

*1. Name of d (G-pPL)	leposit (micro A-HFIF-6	organism, cel 7-126MI)	ll, seed, plas	smid, etc.)	Escher	ichia c	oli M	5219 ————	
2. Strain desi	gnation given	by the depos	sitor (numb	er, symbols	etc.)		HFIF-H	I	
4. Is this a re Treaty? (If	equest for a f	conversion of ATCC design	a deposit	already at t Yes, AT	he ATCC CC 318	to meet the	requiren	nents of the Bud	apest
5. Is this depo					No				
6. Details and also, where	conditions: a mixture of the methods perm.	necessary for f microorgan itting the che	the cultivations is dep	ation of the	puons o	or its storage	onents of	r testing its via the mixture an	bility and
	see at	tached s	heets						
			,	operties.	De DO2	T L O I E E	пот а	nvironment, or a nware of ar o health c	
environ		.c scrar	ii wiiICii	are or	may b	e dange	rous t	o health o	or
a. For cell (if so list	culture depos t the antibioti ridoma depos	sits please cor	mplete. Is th	e cell being	cultured in	the presence	e of antib	()	
'9 Is this steeler.	المانية	no picase cor	no.	it is the isoty	ype of anti	body produc	œd?		
9. Is this strain a 10. Does this stra If so, what ph Guidelines inv	in contain pla vsical contain	smids relevan	nt to the par	ent process	?	es		nstitutes of Heal	ıh
The answers to the	ese question:	are recomm	ended but n	ot required.		,,.			
			FOR A						
		rcc design					_		
		ATE CULTUR					_		
	D	ATE VIABILI	TY TEST CO	MPLETED			_		
							1		

AMERICAN TYPE CULTURE COLLECTION

12301 PARKLAWN DRIVE ROCKVILLE, MARYLAND 20852

February 27, 1981

James F. Haley, Jr., Esq. Attorney for Biogen N.Y. c/o Fish & Neave 277 Park Avenue New York, New York 10172

2000

Gentlemen:

We received on February 26, 1981 a deposit of cultures of organisms identified as Escherichia coli M5219(G-pPLa-HFIF-67-12\Delta MI), HFIF-H, and Escherichia coli HB101(p \(\text{D325}\)]-qHFIF-4), HFIF-I.

These strains have been assigned the ATCC numbers 31824 and 31825, respectively.

We understand that these organisms are being deposited in the American Type Culture Collection (ATCC) in connection with the filing of an application for a patent.

We further understand that the deposit of these cultures does not grant to ATCC during the effective term of the patent anticipated a license, either expressed or implied to infringe the patent, and our release of these cultures to others does not grant them a license, either expressed or implied, to infringe the patent.

We further understand that if these cultures should die or be destroyed during the effective life of the patent it shall be your responsibility to replace them with living cultures of the same organisms.

We agree in consideration for a one-time service charge, not to distribute these cultures or any information relating thereto or to their deposits until such time as a patent has been issued disclosing the above deposits except in accordance with a U.S. Patent Office Rule of Practice, Rule 14, or until you authorize us to make these strains available. After a patent is issued and we are so informed the cultures will be made available for distribution to the public. The ATCC agrees to maintain the cultures for a period of 30 years from the deposit date. Non-payment of the service charge within 90 days of the deposit date relieves the ATCC from the above provisions.

Payment in the amount of \$1,140.00 received. Thank you.

Sincerely yours.

By: (Mrs.) Bobbie A. Brandon

Inteline A. Browlan

An independent non-profit organization incorporated in Washington, D. C. and devoted to the preservation of reference cultures and their distribution to the scientific community.

1.	Scientific name of organism E.coli M5219(G-oPIa-HFJF-67-126MI)	Do not write in this box
2.	Strain designations other than ATCC number HFIF+H	ATCC 1 3/22!!-
	Is this the type strain of this organism (see reverse side)? NO	Accession date 2/26/91
h.	If this strain has been designated in the literature as the type strain, please cite reference:	Date received 2/36/8
5.	Hame and address of depositor: Biogen N.V. 15 Pietermaai Curacao, Netherlands Antil	les
6.	Isolated by	
	from date	
7.	If you did not isolate this strain, indicate from whom you received if:	
	ATCC depositor	
8.	Reason for deposit:	
	Requested by ATCC Subspecies	
	Produces the antibiotic Assey of	
	Production of Other	Patent
9.	Haintenance: Hedium (attach formula) LB Broth or bactotryptone	
	Temperature 28°C Other LB Broth supplemented	with 50 µg/ml Kanamyci
10.	a) Does this organism survive: Freeze drying? Yes Freezing? b) Recommended method for long-term preservation: Freeze drying or LB Broth/glycerol or DMSO at -	
11.	Is this strain zoopathogenic? NO If so, would you classify it as cla (see reverse side for description	ss 2, 3, or 4?
12.	Is this strain phytopathogenic? NO (Information required by Plant Quara If so, a) Is the geographical distribution of this organism general, lim b) Would you recommend that this strain be made available to any investigator regardless of his location? c) If not, what limits would you place on the distribution of this	ited, or unknown (encircle)? qualified
13.	Please attach a complete description of this strain unless description is reprint.	given in accompanying
14.	References (Please enclose two (2) of each pertinent reprint, if available):
		•
15.	Comments:	
	Do not heat above 28°C.	D. Helen
ATCC	Form 1-B (1971)	for Biogen N.V.
نخب		

COLLECTION OF BACTERIA

1.	Scientific name of organism E.CO11 HB101(D[325]-GHFIF-4) Do not units in this box
2.	Strain designations other than ATCC number HFIF-I ATCC # 3/835
3.	Is this the type strain of this organism (see reverse side)? NO Accession date 2/26/3/
4.	If this strain has been designated in the literature as the type strain, please cite reference: Date received 2/24/8/
5.	Name and address of depositor: Biogen N.V. 15 Pietermaai Curacao, Netherlands Antilles
6.	Isolated by
	from date
7.	If you did not isolate this strain, indicate from whom you received it:
	ATCC depositor
8.	Reason for deposit: Requested by ATCC Subspecies
	Produces the antibiotic Assay of
	Production ofOther Patent
9.	Maintenance: Medium (attach formula) LB Broth or bactotryptone
	Temperature other LB Broth supplemented with 100 mg/ml carbenic
ο.	lin and/or 10 µg/ml tetracycline. a) Does this organism survive: Freeze drying: Yes (poorly) b) Recommended method for long-term preservation:
1.	Freeze drying or LB Broth/glycerol or DMSO at -80°C Is this strain zoopathogenic: NO If so, would you classify it as class 2, 3, or 4:
••	(see reverse side for description of classes)
2.	Is this strain phytopathogenic? NO (Information required by Plant Quarantine Division, USDA) If so, a) Is the geographical distribution of this organism general, limited, or unknown (encircle)? b) Would you recommend that this strain be made available to any qualified investigator regardless of his location? c) If not, what limits would you place on the distribution of this strain?
3.	Please attach a complete description of this strain unless description is given in accompanying reprint.
۱.	References (Please enclose two (2) of each pertinent reprint, if available):
5.	Comments:
	Ja J. Halen Je
rcc	Form 1-B (1971) Attorney for Biogen N.V.

ROBERT C. HORGAN KENNETH B. HERMAN EDWARD F. MULLOWNEY ROBERT R. JACKSON JESSE J. JENNER EDWARD BAILEY DAVIDJ. LEE PATRICIA A MARTONE

KEVIN J. CULLIGAN GLENN A. OUSTERHOUT SUSAN PROGOFF MARGARET A. PIERRI RON E. SHULMAN DOUGLAS J. GILSERT DENISE L. LORING JEPPREY H. INGERMAN

TELECOPIER: (212) 715-0674

October 16, 1991

FREDERICK P. FISH 1855-1930 CHARLES MEAVE 1867-1937

> Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH Mascheroder Weg 1b D-3300 Braunschweig Federal Republic of Germany

JOHN M HINTZ JOHN R. STORELLA WILLIAM J. McCABE JOHN M. DESMARAIS VICKI S. VEENKER LESLIE A. MCOOHELL CHRISTOPHER P. GODZIELA

DAVID C. PLACHE JANE A. MASSARO DUANE-DAVID HOUGH MITCHELL P. SROOK

EDWARD J. DEFRANCO

MARK D. ROWLAND
PHILIPPE Y. RIESEN
MARK D. ENGELMANN
ERIC R. NUSBARD
DAYID A. LOEWENSTEIN
JOHN J. CASSINGHAM
LINDA A. WADLER
REFLEY!

MARK D. ROWLAND

MARTA E. GROSS

NICOLAA, PIBANO DONALD K. REEDY GABRIELLE E. HIGGINS GABRIELLE MIDGINS
JENNIFERN NALL
DONALD L. RHOADS
ELIZABETH M. ALDRIDGE
CLAYS. WILSON
BRENDA J. PANICHI
JEREMY LACK
EVAN M. GSELI
JAMES P. SERGIN
RONALD A. KRASNOW
JEFFREY M. MERSH
LIANNA C. KALMAR
SRADFORD L. FRIEDMAN
DESRA A. SONTEMPO
LORETTA. MIRAGLIA
MOREY S. WILDES
CHRISTOPHER J. NARMETT
MARIE N. MACNICNOL
WILLIAM A. SCHONEMAN

Biogen - B8/B8 CIP Deposits DSM 1791-1793; 1851-1854

Dear Sir:

We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,

James F. Haley, Ivor R. Elrifi

Attorneys for Biogen, Inc.

JFH/IRE:bb Enclosures To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GMBH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

To be fi	illed in by the Depositary Authority	
DSM-A	Accession number :	
Date	cultura recaived :	į
		1
		1

BACTERIA/FUNGI

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.1^2

Identification reference ³ : HFIF-F	The culture to be deposited is :
M5219 (G-pPLa-HFIF-67-12Δ19) Taxonomic designation :	(X) a pure cultura
	() a mixture of microorganisms
Escherichia coli	(Mark with a cross where applicable)
1. CONDITIONS FOR CULTIVATION	(X) ⁵
Medî um:	pH before sterilisation :
	Sterilisation min at °C
as according to original deposit application DSM 1853	pM after sterilisation:
	Oxygen relationship :
	() merobic
	() micromerophilic
	() obligate anaerobic
	Specific gaseous requirements :
	Incubation temperature: +C
	Incubation time:
	Short term storage at: •C
	Interval of transfer:

Number, symbols etc., given to the microorganism by the depositor.

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/Fungi (first page) 0488

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

Nukleinsauren" (5. überarbeitete Fassung BMFT)

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the microorganism be indicated.

V. CONDITIONS FOR TESTING VIABILITY	(_X) ⁵
COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(x) ⁵
cription of components:	
od(s) for checking presence of components:	

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1 Bacteria/Fungi (second page) 0488

	THE STRAIN HAS	TO BE HANDLED UNDE	R THE FOLLOWING	LABORATORY (CONTAINMENT LEVEL':	
	() L1		() L2		
	() L3		() 14		
	IC THIC CTRAIN	DANCEDONE TO UTAL				
	(if yes, please	DANGEROUS TO HEALT!	OR THE ENVIRON	MENT ?	() YES	(X) NO
	() yes, presse	specify:)				(X) ⁵
	(X) the un	ndersigned is not a	ware of such pro	perties		
1	F THE MICROORGA	NISM IS GENETICALLY	MANIPULATED:			
1	. PLEASE INDICA	TE ALL THE RELEVANT	GENETIC PROPER	TIES:		
	general genet	ic recombination (r	ec):			
	sensitivities	:				
	resistances:					
	modifications	:				
	restrictions:					
	auxotrophies:					
2.	. DESIGNATION OF	THE DONOR ORGANISM	I(S), THE DNA OF	WHICH HAS BE	EN CLONED INTO THE P	LASMID:
		whether (WITHOUT A			ake appropriate step ional guidelines.) ESTIONS THE ORGANISM	
	1. THE SUBGENO	MIC FRAGMENTS OF TH	E DNA DEFINETLY	HAVE NO PATHO	OGENIC POTENTIAL.	
	() YES					
	2. THE SUBGENOR	MIC FRAGMENTS HAVE	A PATHOGENIC POT	ENTIAL.		
	() YES					
	IN THE LATTER	CASE PLEASE NOTE:				
						pipulated, potentially (or by an equi-

58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. überarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

2KBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

Form DSM-BP/1-Bacteria/Fungi (third page) 0488

VIII. A	DDITIONAL DATA	()8	
C. DEPOS		Jan d. Haling	
: :	Biogen, Inc.	James F. Haley, Jr. Ivor R. Elrifi Attorneys for Biogen	, Ir
dress:	14 Cambridge Center Cambridge, Massachusetts 02142	Fish & Neave 875 Third Avenue New York, New York	

Mark with a cross if additional information is given on an attached sheet. It is strongly recommended that the scientific description and/or proposed taxonomic designation (see I.)

The name of the depositor must be identical with the signature. In case of a legal entity the signatures of two representatives, officially nominated by this entity, are

where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

of the microorganism be indicated.

Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).

DEUTSCHE SAMPLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GRIDH Mascheroder Weg 1b 0-3300 Braumschweig Federal Republic of Germany

To be filled in by the Depositary Authority	
DSM-Accession number :	
Date culture received :	
	- 1

BACTERIA/FUNGI

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.12

Identification reference ³ : HFIF-A HBl01(G-pBR322(Pst)/HFIF 3) Taxonomic designation : Escherichia coli	The culture to be deposited is: (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION	(X) ⁵
ledium:	pH before sterilisation :
as according to original	Sterilisation min at *C
deposit application for DSM 179	pH after sterilisation:
	Oxygen relationship:
	() aerobic
	() microaerophilic
	() obligate anaerobic
	Specific gaseous requirements :
	Incubation temperature: *C
	Incubation time:
	Short term storage at: •C
	Interval of transfer:

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment Level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/Fungi (first page) 0488

CONDITIONS FOR TESTING VIABILITY	(x) ⁵
CMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(x) ⁵
ription of components:	
d(s) for checking presence of components:	

Form DSM-BP/1 Bacteria/Fungi (second page) 0488

THE	STRAIN HAS TO BE	HANDLED UNDER THE FO	LLOWING LAB	ORATORY CONT	AINMENT LEVEL ¹ :	
() L1		()	L2		
() L3		()	L4		
IS TH	IS STRAIN DANGER	OUS TO HEALTH OR THE	ENVIRONMENT	• •	() YES	(X) NO
	es, please speci			•	() / / / / /	(x) ⁵
(x) the undersi	ned is not aware of s	such proper	ties		·
IF THE	MICROORGANISH I	S GENETICALLY MANIPUL	ATED:			
1. PLE	ASE INDICATE ALL	THE RELEVANT GENETIC	PROPERTIES	3:		
ger	eral genetic rec	ombination (rec):				
sen	sitivities:					
res	istances:					
mod	ifications:					
res	trictions:					
aux	otrophies:					
2. DES	IGNATION OF THE I	DONOR ORGANISM(S), THE	E DNA OF WH	ICH HAS BEEN	CLONED INTO THE P	LASHID:
Plea	ogenic potentia:	netically manipulated ((see: ZKBS guideline (WITHOUT A DEFINIT	s or equiv	/alent nation	s muidalises \	
1. 1	HE SUBGENOMIC FR	AGMENTS OF THE DNA DE	FINETLY HAV	E NO PATHOGE	NIC POTENTIAL.	
() YES					
2. 1	HE SUBGENOMIC FR	AGMENTS HAVE A PATHOG	ENIC POTENT	TAL.		
() YES					
IN	THE LATTER CASE	PLEASE NOTE:				
par	nogenic organism ent national bio	gulations of the ZKBS is for deposition when logical safety commis	a copy of	the permit i	ssued by the 7KRS	pipulated, potentially (or by an equi- les the deposition
The C	SM colv secones	for deposit microorga	-:			

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. überarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. ADC	VIII. ADDITIONAL DATA		8 _{ر)}
IX. DEPOS	itok ⁹		
Hame:	Biogen, Inc.	Signatu	James F. Haley, Jr.
Address:	14 Cambridge Center Cambridge, Massachusetts	Date: 02142	Ivor R. Elrifi Attorneys for Biogen, Inc Fish & Neave 875 Third Avenue New York, New York 10022
			10/18/91

Mark with a cross if additional information is given on an attached sheet. It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.)

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

of the microorganism be indicated. Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional). The name of the depositor must be identical with the signature.

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GMbH
Mascheroder Weg 1b
D-3300 Braunschweig
Federal Republic of Germany

be filled in by the Depositary Authority	
DSM-Accession number :	
Date culture received :	
	DSM-Accession number :

BACTERIA/FUNGI 1

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.12

Identification reference ³ :	The culture to be deposited is :
HFIF-B	
HB101(G-pBR322(Pst)/HFIF 6) Taxonomic designation :	(X) a pure culture
Escherichia coli	() a mixture of microorganisms
Escherichia Coli	(Mark with a cross where applicable)
1. CONDITIONS FOR CULTIVATION	(x) ⁵
edium:	pH before sterilisation :
	Sterilisation min at *C
as according to original deposit application for DSM 1792	pH after sterilisation:
approach for bon 1792	Oxygen relationship:
	() aerobic
	() micromerophilic
•	() obligate anaerobic
•	Specific gaseous requirements :
	Incubation temperature: •c
	Incubation time:
	Incubation time: Short term storage at: *C

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

Nukleinsauren" (5. uberarbeitete Fassung BMFT)

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the microorganism be indicated.

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/Fungi (first page) 0488

V. CONDITIONS FOR TESTING VIABILITY	(x) ⁵
COMPONENTS OF MINES OF MINES	
COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(_x) ⁵
cription of components:	
nod(s) for checking presence of components:	
presente of components:	

THE STRAIN HAS TO BE HANDLED UNDER	THE FOLLOWING LABORATORY CONTAIN	MMENT LEVEL 1:	
() L1	() L2		
() L3	() L4		
IS THIS STRAIN DANGEROUS TO HEALTH ((if yes, please specify:)	OR THE ENVIRONMENT ?	() YES	(_Х) мо (Х) ⁵
(X) the undersigned is not awa			
F THE MICROORGANISM IS GENETICALLY I			
. PLEASE INDICATE ALL THE RELEVANT			
general genetic recombination (rec	:):		
sensitivities:			
resistances:			
modifications:			
restrictions:			
auxotrophies:			
DESIGNATION OF THE DONOR ORGANISMOS	S), THE DNA OF WHICH HAS BEEN CLO	ONED INTO THE P	LASMID:
If the strain is genetically manipu pathogenic potential (see: ZKBS gui Please specify whether (WITHOUT A D FOR DEPOSITION).	plated the depositor must take ap delines ⁵ or equivalent national EFINITE ANSWER TO THESE QUESTION	opropriate step: guidelines.) IS THE ORGANISM	s to prove any CANNOT BE ACCEPTED
1. THE SUBGENOMIC FRAGMENTS OF THE	DNA DEFINETLY HAVE NO PATHOGENIC	POTENTIAL.	
() YES			
2. THE SUBGENOMIC FRAGMENTS HAVE A I	PATHOGENIC POTENTIAL.		
() YES		•	
IN THE LATTER CASE PLEASE NOTE:			
According to the regulations of the pathogenic organisms for deposition valent national biological safety of form	e ZKBS ⁶ the DSM can only accept on when a copy of the permit issu commission) for work on the organ	genetically man ed by the ZKBS ^O nisms accompani	ipulated, potentially (or by an equi- es the deposition

58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. uberarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

Form DSM-BP/1-Bacteria/Fungi (third page) 0488

VIII. AL	DDITIONAL DATA	()8
IX. DEPO	sitor ⁹	
Name:	Biogen, Inc.	Signature: J. D. L. D. L. J. James F. Haley, Jr. Ivor R. Elrifi
Address:	14 Cambridge Center Cambridge, Massachusetts 02142	Attorneys for Biogen, Date: Fish & Neave 875 Third Avenue New York, New York

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

Herk with a cross if additional information is given on an attached sheet. It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.

Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).

The name of the depositor must be identical with the signature.

To
DEUTSCHE SAMMLUNG VON MIKROORGANISMEN
UND ZELLKULTUREN GRBH
Mascheroder Weg 1b
D-3300 Braumschweig
Federal Republic of Germany

To	be filled in by the Depositary Authority	
	DSM-Accession number :	
	Date culture received :	

BACTERIA/FUNGI

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.12

Identification reference ³ : HFIF-C HB101(G-pBR322(Pst)/HFIF 7) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is: (X) a pure culture () a mixture of microorganisms
I. CONDITIONS FOR CULTIVATION	(Mark with a cross where applicable)
edium:	pH before sterilisation :
as according to original deposit application for DSM 1793	Sterilisation min at *C pH after sterilisation: Uxygen relationship: () merobic () micromerophilic () obligate anmerobic Specific gaseous requirements:
	Incubation temperature: *C
	Short term storage at: °C Interval of transfer:

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Mukleinsäuren" (5. überarbeitete Fassung BMFT)

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is strontly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the microorganism be indicated.

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/Fungi (first page) 0488

. CONDITIONS FOR TESTING VIABILITY	(xo ⁵
COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(x) ⁵
cription of components:	
od(s) for checking presence of components:	

Form DSM-BP/1 Bacteria/Fungi (second page) 0488

THE STRAIN HAS TO BE HANDLES UND	ER THE FOLLOWING LABORATORY CO	MTAINMENT LEVEL 1:	
() L1	() L2		
() В	() L4		
IS THIS STRAIN DANGEROUS TO HEALT	H OR THE ENVIRONMENT ?	() YES	(X) NO
(if yes, please specify:)			(X) ⁵
(X) the undersigned is not a	aware of such properties		
IF THE MICROORGANISM IS GENETICALL			
1. PLEASE INDICATE ALL THE RELEVAN	T GENETIC PROPERTIES:		
general genetic recombination (rec):		
sensitivities:			
resistances:			
modifications:			
restrictions:			
auxotrophies:			
2. DESIGNATION OF THE DONOR ORGANIS	SM(S), THE DNA OF WHICH HAS BEI	EN CLONED INTO THE PI	LASHID:
 If the strain is genetically man pathogenic potential (see: ZKBS Please specify whether (WITHOUT FOR DEPOSITION). 	QUIDELINES OF ACHIVELANT NATI	cool ouidaliana \	
1. THE SUBGENOMIC FRAGMENTS OF T	HE DNA DEFINETLY HAVE NO PATHO	GENIC POTENTIAL.	
() YES			
2. THE SUBGENOMIC FRAGMENTS HAVE	A PATHOGENIC POTENTIAL.		
() YES			
IN THE LATTER CASE PLEASE NOTE:			
According to the regulations of pathogenic organisms for deposi valent national biological safe form	TION WHEN A CORY Of the Decimit	iccured by the 7racy	/ / o o but an armit
The DSM only accepts for deposit (58956 (Beiblatt 1) Teil 1, Medizin	microorganisms which belong to	hazard group [or [I, according to DIN

^{58956 (}Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. überarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. A	DOITIONAL DATA		()8
IX. DEPO	SITOR ⁹	=		
Name:	Biogen, Inc.		JIJI I	11
Address:	14 Cambridge Center Cambridge, Massachusetts 02142	Iv At	or R. Elr torneys f Fish & Nea 875 Third	ifi or Biogen, ave

Mark with a cross if additional information is given on an attached sheet.

It is strongly recommended that the scientific description and/or proposed taxonomic designation (see I.) of the microorganism be indicated.

required.

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional). The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are

To DEUTSCHE SAMPLUNG VON HIKROORGANISHEN UND ZELLKULTUREN GRON Mascheroder Weg 1b D-3300 Braunschweig Federal Republic of Germany

be filled in	by the Depositary Authority
DSM-Accessio	n number :
Date culture	received :
Date Cutture	LecalAed :

BACTERIA/FUNGI 1

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED MEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN MILE OF 12

1. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ :	The culture to be deposited is :
HFIF-G	
M5219 (G-pPLc-HFIF-67-8)	(X) a pure culture
exonomic designation :	() a mixture of microorganisms
Escherichia coli	(Mark with a cross where applicable)
. CONDITIONS FOR CULTIVATION	(x) ⁵
ium:	pH before sterilisation :
	Sterilisation min at •c
as according to original deposit application DSM 1854	pH after sterilisation:
	Oxygen relationship:
	() merobic
	() microserophilic
·	() obligate anaerobic
·	Specific gaseous requirements :
	Incubation temperature: •c
	Incubation time:
	Short term storage at: •C
	Interval of transfer:

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Mukleinsäuren" (5. überarbeitete Fassung BMFT)

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the microorganism be indicated.

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/Fungi (first page) 0488

ONDITIONS FOR TESTING VIABILITY	(X) ⁵
ONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(X) ⁵
tion of components:	()
for checking presence of components:	

Form DSM-BP/1 Bacteria/Fungi (second page) 0488

THE STRAIN HAS TO BE HANDLED UNDER THE F	OLLOWING LABORATORY CO	NTAINMENT LEVEL 1:	
() L1	() L2		
() L3	() L4		
IS THIS STRAIN DANGEROUS TO HEALTH OR THE	ENVIRONMENT ?	() YES	(X) NO
(X) the undersigned is not aware of			
			
1. PLEASE INDICATE ALL THE RELEVANT GENET!	IC PROPERTIES:	•	
general genetic recombination (rec):			ı
Sensitivities:			
resistances:			
modifications:			
restrictions:			
auxotrophies:			
2. DESIGNATION OF THE DONOR ORGANISM(S), TO	HE DNA OF WHICH HAS BEI	EN CLONED INTO THE F	PLASMID:
 If the strain is genetically manipulated pathogenic potential (see: ZKBS guideling Please specify whether (WITHOUT A DEFINITION). 	nes" or equivalent nati	ional muidalines \	
1. THE SUBGENOMIC FRAGMENTS OF THE DNA D	EFINETLY HAVE NO PATHO	GENIC POTENTIAL.	
() YES			
2. THE SUBGENOMIC FRAGMENTS HAVE A PATHO	GENIC POTENTIAL.		
() YES			
IN THE LATTER CASE PLEASE NOTE:			
According to the regulations of the ZKB pathogenic organisms for deposition whe valent national biological safety commit form	n a copy of the permit	issued by the 7000	0 /or by an and
The DSM only accepts for denosit microord			

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIM 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBM 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. überarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. A	ODITIONAL DATA		8 _()
IX. DEPO	SITOR ⁹		
			
Name:	Biogen, Inc.	Signatu	re: For folial
			James F. Haley, Jr/ Ivor R. Elrifi
			Attorneys for Riogen, Inc
Address:	14 Cambridge Center Cambridge, Massachusetts 02142	Date:	Fish & Neave 875 Third Avenue New York, New York 10022
			10/13/31

Mark with a cross if additional information is given on an attached sheet. It is strongly recommended that the scientific description and/or proposed taxonomic designation (see I.)

of the microorganism be indicated.

Nark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).

The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

DEUTSCHE SAMMLUNG VON MIKROORGANISHEN UND ZELLKULTUREN GRIDH Mescheroder Weg 1b 0-3300 Braunschweig Federal Republic of Germany

To be filled in by the Depositary Authority	
DSM-Accession number :	
Date culture received :	
	İ

BACTERIA/FUNGI

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.12

Identification reference ³ :	The culture to be deposited is:
HFIF-D	(X) a pure culture
M5219 (G-pPLa-HFIF-67-12) Taxonomic designation :	
rexormine designation :	() a mixture of microorganisms
Escherichia coli	(Mark with a cross where applicable)
II. COMDITIONS FOR CULTIVATION	(_X) ⁵
Medium:	pH before sterilisation :
as according to original deposit application for DSM 1851	Sterilisation min at °C
	pH after sterilisation:
	Oxygen relationship:
	() merobic
	() microaerophilic
	() obligate anaerobic
	Specific gaseous requirements :
	Incubation temperature: •C
	Incubation time:
	Short term storage at: •C
	Interval of transfer:

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsäuren" (5. überarbeitete Fassung BMFT)

MURICEITSaurer (3. uperarbeitete rasaury onr),

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the microorganism be indicated.

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/Fungi (first page) 0488

. CONDITIONS FOR TESTING VIABILITY	(X) ⁵
COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	
THE STATES (WICH APPLICABLE)	(X) ⁵
ription of components:	
•	
•	
od(s) for checking presence of components:	

() L1 () L2 () L3 () L4 IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT? () YES (X) MO (if yes, please specify:) (X) ⁵ (X) the undersigned is not aware of such properties IF THE MICROORGANISM IS GENETICALLY MANIPULATED: 1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES: general genetic recombination (rec): sensitivities: resistances: modifications: restrictions: auxotrophies: 1. DESIGNATION OF THE DONOR ORGANISM(S), THE DMA OF UNICH MAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKS guidelines* or equivalent national guidelines.) Please specify whether (MITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENONIC FRAGMENTS OF THE DMA DEFINETLY MAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENONIC FRAGMENTS NAVE A PATHOGENIC POTENTIAL. () YES	THE STRAIN HAS TO BE HANDLED UNDER THE FOLLO	DVING LABORA	TORY CONTA	IMMENT LEVEL 1:	
IS THIS STRAIN DANGEROUS TO MEALTH OR THE ENVIRONMENT? () YES (X) NO (if yes, please specify:) (X) (X) the undersigned is not aware of such properties IF THE MICROORGANISM IS GENETICALLY MANIPULATED: 1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES: general genetic recombination (rec): sensitivities: resistances: modifications: restrictions: auxotrophies: DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZESS guidelines) or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY MAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.	() L1	() L	2		
(if yes, please specify:) (X) the undersigned is not aware of such properties If THE MICROORGAMISM IS GENETICALLY MANIPULATED: PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES: general genetic recombination (rec): sensitivities: resistances: modifications: restrictions: auxotrophies: DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASHID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZXBS guidelines) or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE AMSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY MAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.	() L3	() L	•		
IF THE MICROORGANISM IS GENETICALLY MANIPULATED: 1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES: general genetic recombination (rec): sensitivities: resitances: modifications: restrictions: auxotrophies: DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines* or equivalent national guidelines.) Please specify whether (MITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.		VIRONMENT ?		() YES	
general genetic recombination (rec): sensitivities: resistances: modifications: restrictions: auxotrophies: DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines) or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.			.		
general genetic recombination (rec): sensitivities: resistances: modifications: restrictions: auxotrophies: DESIGNATION OF THE DOMOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). The Subgenomic fragments of the DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES The Subgenomic fragments have a Pathogenic Potential.					
resistances: modifications: restrictions: auxotrophies: DESIGNATION OF THE DOMOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines) or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.		ROPERTIES:			
resistances: modifications: restrictions: auxotrophies: DESIGNATION OF THE DONOR ORGANISM(S), THE DMA OF WHICH HAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DMA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.					
modifications: restrictions: auxotrophies: DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines) or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL. () YES	sensitivities:				
restrictions: auxotrophies: DESIGNATION OF THE DOMOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE GUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.	resistances:			·	
auxotrophies: DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines) or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL. () YES	modifications:				
DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID: If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines) or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL. () YES	restrictions:				
If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL. () YES	auxotrophies:				
Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION). 1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL. () YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL. () YES	. DESIGNATION OF THE DONOR ORGANISM(S), THE DI	NA OF WHICH	HAS BEEN C	LONED INTO THE	: PLASMID:
() YES 2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL. () YES	Please specify whether (WITHOUT A DEFINITE A	OF SOUNDER	At Bations	l a nidalimaa \	
2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL. () YES	1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFIN	ETLY HAVE N	O PATHOGEN	IC POTENTIAL.	
() YES	() YES				
	2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENI	C POTENTIAL	-		
	() YES				
IN THE LATTER CASE PLEASE NOTE:	IN THE LATTER CASE PLEASE NOTE:				
According to the regulations of the ZKBS ⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS ⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form	pathogenic organisms for deposition when a valent national biological safety commission	copy of the	permit is	cuert hu the 71'	RCO (or by on any

Sepse (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. überarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

2KBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. AD	DITIONAL DATA		8ر)
IX. DEPOS	sitor ⁹		
Name:	Biogen, Inc.	Signatu	James F. Haley, Jr.
Address:	14 Cambridge Center Cambridge, Massachusetts 02142	Date:	Ivor R. Elrifi Attorneys for Biogen, Inc Fish & Neave 875 Third Avenue New York, New York 10022

Mark with a cross if additional information is given on an attached sheet.

It is strongly recommended that the scientific description and/or proposed taxonomic designation (see I.) of the microorganism be indicated.

of the microorganism be indicated.

Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when o drafting the proposed taxonomic designation (The supplying of such information is optional).

The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are

required.

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GIRDH Mascheroder Weg 1b D-3300 Braunschweig Federal Republic of Germany

To be filled in by the Depositary Authority	
DSM-Accession number :	
Date culture received :	- 1
	- 1
	- 1
	- [

BACTERIA/FUNGI

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN RULE 9.12

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-E K12ΔHI (G-pPLa-HFIF-67-12)	The culture to be deposited is: (X) a pure culture
Taxonomic designation ⁶ : Escherichia coli	() a mixture of microorganisms (Mark with a cross where applicable)
II. CONDITIONS FOR CULTIVATION	(x) ⁵
ledium:	pH before sterilisation :
as according to original deposit application for DSM 1852	Sterilisation min at *C pH after sterilisation: Oxygen relationship: () merobic () micromerophilic () obligate anaerobic Specific gaseous requirements:
	Incubation temperature: •c
	Short term storage at: •C Interval of transfer:

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. überarbeitete Fassung BMFT)

NUKLEINSAUTEN (3. uperarbeitete rassung pri).

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/Fungi (first page) 0488

CONDITIONS FOR TESTING VIABILITY	(* 2 ⁵
MENTS OF MIXED CULTURES (WHEN APPLICABLE)	(x) ⁵
ion of components:	
) for checking presence of components:	
the sheeking presence of components:	

Form DSM-BP/1 Bacteria/Fungi (second page) 0488

THE STRAIN HAS TO BE HANDLED UNDER THE	FOLLOWING LABORATORY CON	TAINMENT LEVEL 1:	
() L1	() L2		
() L3	() L4		
IS THIS STRAIN DANGEROUS TO HEALTH OR TH	HE ENVIRONMENT ?	() YES	(x) NO
(X) the undersigned is not aware o			
IF THE MICROORGANISM IS GENETICALLY MANIE			
1. PLEASE INDICATE ALL THE RELEVANT GENET	TIC PROPERTIES:		
general genetic recombination (rec):			
sensitivities:			
resistances:			
modifications:			
restrictions:			
auxotrophies:			
2. DESIGNATION OF THE DONOR ORGANISM(S), 1	THE DNA OF WHICH HAS BEEN	CLONED INTO THE P	LASNID:
 If the strain is genetically manipulate pathogenic potential (see: ZKBS guideli Please specify whether (WITHOUT A DEFIN FOR DEPOSITION). 			
1. THE SUBGENOMIC FRAGMENTS OF THE DNA	DEFINETLY HAVE NO PATHOGE	NIC POTENTIAL.	
() YES			
2. THE SUBGENOMIC FRAGMENTS HAVE A PATH	OGENIC POTENTIAL.		
() YES			
IN THE LATTER CASE PLEASE NOTE:			
According to the regulations of the ZKI pathogenic organisms for deposition who valent national biological safety comm form			

^{58956 (}Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. überarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VIII. AL	DOITIONAL DATA	()8
IX. DEPO	SITOR ⁹	
lame:	Biogen, Inc.	Signature: JA 15/5/ James F. Haley, Jr.
ddress:	14 Cambridge Center Cambridge, Massachusetts 02142	Ivor R. Elrifi Attorneys for Biogen, I Fish & Neave 875 Third Avenue New York, New York 100

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required. Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

Mark with a cross if additional information is given on an attached sheet. It is strongly recommended that the scientific description and/or proposed taxonomic designation (see I.)

of the microorganism be indicated.

8 Hark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional). The name of the depositor must be identical with the signature.

(Please mark what applies)

	Temperature:	28°	C		
	Incubation t Short-term s Interval of	torage at	4°c Nave	r exc	cee
	Liquid culture stationary Agar culture plate sla]shaker [] ⊠		
Lara hara ar	Any other met	hod:		•	
Long term preservation: Freeze drying ,liquid nitrogen storage	☒	other (pleas	e specify)		
Pre-drying/freezing medium:	·	% :			
Time and temperatur of incubation:					٠.
Suspending fluid:					
Recovery medium: (Viability testing)		j.			
Additional remarks:					
•	٠				

Gent 4 June 1980

WESailey

Signature of depositor Afforney for BIOGEN N.V.

(Please mark what applies)

	Temperature: 28°C Incubation time: Short-term storage at 4°c Interval of transfer: Never exceed
	Liquid culture stationary shaker
	Any other method:
freeze drying ,liquid nitrogen storage	other (ple se specify)
Pre-drying/freezing medium:	
Time and temperatur of incubation:	
Suspending fluid:	
Recovery medium: (Viability testing)	A:
Additional remarks:	

4 June 1980

Signature of depositor ()
Attorney for BIOGEN N.V.

(Please mark what applies)

in accordance with the conditions as specified by the depositor on enclosed separate

sheet.

	Incubation time: Short-term storage at 4 °C Interval of transfer: Never exceed Liquid culture stationary shaker Agar culture plate slant stab	2
	Any other method:	
Long term preservation: Freeze drying,liquid nitrogen storage	other (please specify)	
Pre-drying/freezing medium:	·5·:	
Time and temperatur of incubation:		٠,
Suspending fluid:		
Recovery medium:	3. :	
(Viability testing)		
Additional remarks:		
•	,	
	•	

Gent 4 June 1980

Place

date

Signature of depositor

Altorney for BIOGEN N.V.

(Please mark what applies)

in accordance with the conditions as specified by the depositor on enclosed separate \sim

	Incubation time: Short-term storage at 4°C Interval of transfer: Never exceed
	Liquid culture stationary shaker Agar culture plate slant stab
Long term preservation:	Any other method:
Freeze drying ,liquid nitrogen storage	other (please specify)
Pre-drying/freezing medium:	No. 10
Time and temperatur of incubation:	·
Suspending fluid:	
Recovery medium: . (Viability testing))
Additional remarks:	
	•
	•

Gent 4 June 1980

Place

date

Signature of depositor //
Attorney for BIOGEN N.V.

28

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

argenissen.	been deposited with the Deutsche Sammlung von Mikro-
Name and address of depositor:	Biogen N.V. 24 Handelskad Willemsted
•	Curacao, Netherland Antilles
Identification reference of the microorganism used by the depositor:	HFIF-8 HB101(G-pBR322(Pst)/HFIF 6)
Taxonomic designation of the microorganism provi- ded by the depositor:	Escherichia coli
DSM accession number of the microorganism;	DSM 1792
Date of receipt of the viable microorganism:	April 2, 1980 -
In addition to the identification reference of the control of the	ence and the taxonomic designation the depositor XXXX c description of the microorganism.
The microorganism has been sent to	the DSM directly by the depositor.
The microorganism has been sent to depository under the designation as	the DSM on behalf of the depositor by the following nd accession number given:
As stated by the depositor the microogurunder the following conditions: without any restrictions	nism may be rendered accessible to any third party
	e agreement between the European Patent Organisation 5, 301–307, 1978) and/or
according to the Swedish patent leg Patent Office and the DSM (Svensk i	gislation and to the agreement between the Swedish Patenttioning nr 12, 1979)
△ DSH and the German Patent Office (•
and Title 35, United States Code, : X America and b) without any restrict	de of Federal Regulations, section 1.14 (37.DFR 1.14) section 122 (35 U.S.C. 122) of the United States of tion on availability to the public of the culture atent wherein the deposited microorganism is part
X in accordance with the French pates	nt law
in accordance with the conditions sheet.	as specified by the depositor on enclosed separate
Göttingen, April 2, 1980	2 Cour
	SAMMLUNG VON MIKROORGANISMEN Signature
Place date	
Place date	at für Biotechnologische Forschung möhl Grisebachstraße 8 D-3400 Göttingen

Vorsitzender des Aufsichtsrats: Min. Dir. Dr. Friedrich Bischoff

Geschäftsführer: Dr. Maria-Regina Kula Dr. Heimut Zeitträger

Bankkonto: Gebr. Löbbecke, Braunschweig Konto 23 781 (BLZ 270 305 00) Registergericht: Amtsgericht Braunschweig HRB 477

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikro-

Name and address		Biogen N.V.	
of depositor:		24 Handelskad	
		Willemsted	•
			• •
Identification refu	erence of	Curacao, Netherland Anti	lles
the microorganism		HFIF-C	
the depositor:		HB101(G-pBR322(Pst)/HFIF	7)
		p = 000(100),	• •
Taxonomic designati			
the microorganism p ded by the deposito		Escherichia coli	
one by the deposite	MC 2		
OSM accession number	r of	DSM 1793	•
the microorganism;		JJ.1. 1777	
Date of receipt of	tha	A: 1 0 1000	
viable microorgania		April 2, 1980	
	••	•	VVV
In addition to the	identification refere	nce and the texonomic designation the d	epositor has
	brownood a acreustite	description of the microorganism.	
X The microorgan:	ism has been sent to	the DSM directly by the depositor.	
		the DSM on behalf of the depositor by ti	
depository unde	er the designation and	d accession number given:	he following
No obstad by the dea	andhan bha minana		
As stated by the dec	Maitor the micrograph	ism may be rendered accessible to any	aind and
under the following	conditions:		itto beti
without any res	trictions		
and the use (ut	Licial Jonnal ELO 2	agreement between the European Patent (301-307, 1978) and/or	
Recording to the Patent Office a	a Swedish patent legi nd the DSM (Svensk Pa	slation and to the agreement between the stentioning or 12, 1979)	e S ve dish
in accordance w	ith the "Declaration man Patent Office (at	of Release" to be filed by the deposito	r with the
		of Federal Regulations, section 1.14 (
and Title 35. U	nited States Code. se	ection 122 (35 U.S.C. 122) of the United	37.0 K 1.14)
America and b)	Without any restricti	on on availability to the public of the	culture
upon granting o	f a United States pat	ent wherein the deposited microorganism	is part
	re of the invention	•	•
OL FUE GISCIOSA		•	
OL FUE GISCIOSA	ith the French patent	law	
in accordance and	ith the French patent	law specified by the depositor on enclosed	congrate
in accordance and	ith the French patent		separate
in accordance w	ith the French patent		separate
in accordance w.	ith the French patent ith the conditions as		separate
in accordance w	ith the French patent ith the conditions as		separate
in accordance washest. Göttingen, Ap	ith the French patent ith the conditions as	specified by the depositor on enclosed	separate
in accordance washest. Göttingen, Ap	ith the French patent ith the conditions as oril 2, 1980	specified by the depositor on enclosed SAMMLUNG VON MIKROORGANGSMENUTE der	separate Our
in accordance washest. Göttingen, Ap	ith the French patent ith the conditions as oril 2, 1980	specified by the depositor on enclosed SAMMLUNG VON MIKROORGANGSMEDUTE der chaft für Biotechnologische Forschung men	separate Our
in accordance washest. Göttingen, Ap	ith the French patent ith the conditions as oril 2, 1980	SAMMLUNG VON MIKROORGA/GSMEDUTE der chaft für Biotechnologische Forschung mbH Grisebachstraße 8	Separate Our
in accordance washest. Göttingen, Ap	ith the French patent ith the conditions as oril 2, 1980	SAMMLUNG VON MIKROORGA/GSMEDUTE der chaft für Biotechnologische Forschung mbH Grisebachstraße 8	Separate Our
in accordance wheat. Göttingen, Ap	ith the French patent ith the conditions as Fril 2, 1980 ate DEUTSCHE	specified by the depositor on enclosed SAMMLUNG VON MIKROORGANGSMEDUTE der chaft für Biotechnologische Forschung men	<u>Odur</u>
in accordance wheat. Göttingen, Ap	ith the French patent ith the conditions as Fil 2, 1980 Ate DEUTSCHE Gesellsche Forschung mbH, Maschere	SAMMLUNG VON MIKROORGANGSMEDURE der chaft für Biotechnologische Forschung mbH Grisebachstraße 8 D-3400 Göttingert oder Weg 1, 3300 Braunschweig, Tel.: (05 31) 70 08—1.	Telex: 9—5 26 67
in accordance wheat. Göttingen, Ap Place di	ith the French patent ith the conditions as Fril 2, 1980 ate DEUTSCHE	SAMMLUNG VON MIKROORGANGSAGDURE der Chaft für Biotechnologische Forschung mbH Grischachstraße 8 D-3400 Göttingerr oder Weg 1, 3300 Braunschweig, TeL: (05.31) 70.08—1, Bankkonto:	<u>Odur</u>

ALAMUNCEDGETENT UP RELEIPT AND ACCEPTANCE The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorcanismen. BIOGEN N.V. Name and address 24 Handelskad of depositor: Willemsted.

Identification reference of the microorganism used by the depositor:

HFIF-D

M5219 (G-pPLa-HFIF-67-12)

Curacao, Netherland Antilles

Texonomic designation of the microorganism provided by the depositor:

Escherichia coli

DSM accession number of the microorganism:

DSM 1851

Date of receipt of the viable microorganism:

June 5, 1980 _

In addition to the identification reference and the taxonomic designation the depositor NéeX ACCUMATE has not provided a scientific description of the microorganism.

The microorganism has been sent to the DSM directly by the depositor.

The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microoganism may be rendered accessible to any third party under the following conditions:

vitious any restrictions

according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or

according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)

in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)

in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of

X America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention

in accordance with the French patent law

in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5, 1980

Place

date

DELTSCHE SAMMLUNG VON MIKROORGANISKES

der

Gesellschaft für Biotechnologische Forschung möhl Grissbechstreße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbM, Mascheroder Weg 1, 3300 Braunschweig, Teiz (05.31) 70.08-1, Telex: 9-5.25.67

Vorsitzender des Autsichtsrats: Min. Dir. Dr. Friedrich Bischoff

Geschättsführer: Dr. Maria-Regina Kula Dr. Helmut Zeitträger

Bankkonto: Gebr. Löbbecke, Braunschwi Konto 23 781 (BLZ 270 305 00)

Registemericat: Amisgenchi Braunschwerg HRB 477

organismen.		deposited with the Deutsche Sa	malung von Mikro-
Name and address	•	BIOGEN N.V.	
of depositor:		24 Handelskad	
		Willemsted,	
•			
Identification refere		Curacao, Netherland A	ntilles
the microorganism use	d by	HFIF-E	•
the depositor:	J Dy	Kl2aHI (G-pPLa-HFIF-6	7-12)
Taxonomic designation	of	•	•
the microorganism pro-			
ded by the depositor:		scherichia coli	
DSM accession number (of		•
the microorganism;		SH 1852	
Date of receipt of the	_		
viable microorganism:	J	une 5, 1980	
in addition to the ide	ntification reference .	and Ab. A.	
ord ton ssd / bealtication	vided a scientific desc	and the taxonomic designation t cription of the microorganism.	he depositor The
	has been sent to the D	SM directly by the depositor.	
depository under	has been sent to the D the designation and acc	SM on behalf of the depositor (by the following
		ession number given:	
s stated by the deposing con	tor the microoganism m ditions:	may be rendered accessible to an	y third party
vithout any rustri		•	
-		ement between the European Pate -307, 1978) and/or	
Patent Office and	vedish patent legislati the DSM (Svensk Patentt	ion and to the agreement between	
in accordance with DSM and the German	the "Declaration of Re Patent Office (at pres	elease" to be filed by the deposent Form P 2570)	
in accordance with	a) Title 37 Code of E		16 (T7 CCD 1 14)
America and b) with	d States Code, section	122 (35 U.S.C. 122) of the Uni	ted States of
upon granting of a	But any restriction on	availability to the public of	the culture
of the disclosure	f the invention	evailability to the public of the herein the deposited microorgan	uism is part
in accordance with	the French patent law		•
	the conditions as seen	terat by the same	
sheet.	constituts as spec	ified by the depositor on enclo	sed separate
			•
öttingen, June	5,1980		\bigcirc
	DEUTECHE SAMMLU	NG VON MIKROORGANISMEN	July 2
date date		der Signatur	B
•	Gesellechalt für Biou	schnologische Forschung mbH	_
		ebacherzée é	•
		00 Göttingen	
:haft für Biotechnologische For	schung mbH, Mascheroder We	g 1, 3300 Braunschweig, Tel.: (05.31) 70.08	—1. Teles: 9—5 26 67
ider des Aufsichtstats:	Geschäftsführen	Bankkonto:	_
Or. Friedrich Bischoff	Dr. Maria-Regina Kula	Gebr. Löbbecke, Braunschweig	Registerpericht: Amisgericht Braumachwe
	Dr. Helmut Zeitträger	Konto 23 781 (BLZ 270 305 00)	HRB 477

Vors Min.

ACKNOWLEDGEMENT OF REJEIPT AND ACCEPTANCE

The microorganism mentioned below has been organismen.	deposited with	the Deutsche	Sammlung	van Mikro-
ut yer trameri.				

Name and address of depositor:

BIOGEN N.V. 24 Handelskad Willemsted,

Curacao, Netherland Antilles

Identification reference of the microorganism used by the depositor:

HFIF-F

M5219 (G-pPLa -HFIF-67-12A19)

Taxonomic designation of the microorganism provided by the depositor:

Escherichia coli

DSM accession number of the microorganism:

DSM 1853

Date of receipt of the viable microorganism:

June 5, 1980

in addition to the identification reference and the taxonomic designation the depositorXDeX provided / has not provided a scientific description of the microorganism.

- The microorganism has been sent to the DSM directly by the depositor.
- O The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microogenism may be rendered accessible to any third party under the following conditions:

- O without any restrictions
- according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or
- according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)
- in accordance with the "Declaration of Release" to be filed by the depositor with the DSH and the German Patent Office (at present Form P 2570)

in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR I.14)

- and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention
- in accordance with the French patent law
- in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5,1980

Place

date

DEUTECHE SAMMLUNG VON MIKROORGAMISKAMITETUTE

der Gesellschaft für Biotechnologische Forschung mbH Grisebachetraße 8

D-3400 Cöningen-

Gesellschaft für Blotechnologische Forschung mbH. Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05.31) 70.08—1, Telex: 9—5.26.57

Vorsitzender des Aufsichtsrats: Min. Dir. Dr. Friedrich Bischoff

Geschällstührer Dr. Maria-Regina Kula Dr. Helmut Zeitträger

Gebr. Löbbecke, Braunschweig Kanto 23 781 (BLZ 270 305 00) Registergencht: Amisgenchi Braunschweig HRB 477

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address of depositor:

BIOGEN N.V. 24 Handelskad Willemsted,

Curacao, Netherland Antilles

Identification reference of the microorganism used by the depositor:

HFIF-G

M5219 (G-pPlc-HFIF-67-8)

Taxonomic designation of the microorganism provided by the depositor:

Escherichia coli

DSH accession number of the microorganism:

DSM 1854

Date of receipt of the viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositorXHMA 知识知识 / has not provided a scientific description of the microorganism.

igotimes The microorganism has been sent to the DSM directly by the depositor.

The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microoganism may be rendered accessible to any third party under the following conditions:

O without any restrictions

according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or

according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Swemsk Patenttiching nr 12, 1979)

in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)

in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part

of the disclosure of the invention in accordance with the French patent law

in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5,1980

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

Place

date

der

Signature

Gesellechaft für Biotechnologische Forschung mbH Graebachstraße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH. Mascheroder Weg 1, 3300 Braunschweig, TeL: (05.31) 70.08—1, Telex: 9—5.25.67

Vorsitzender des Aufsichtsrats:

Geschältsführer:

Bankkonio:

Remistergericht:

Min. Dir. Dr. Friedrich Bischoff

Or, Maria-Regina Kula Dr. Helmut Zeitträger

Gebr. Loutincke, Braunschweig

Amisgericht Disusschweig HRB 477

Konto 23 781 (BLZ 270 305 00)

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2
To: (Name and Address of Depositor or Attorney)

James F. Haley, Jr., Ivor R. Elrifi Fish & Neave 875 Third Avenue New York, NY 10022

Deposited on Behalf of: Biogen, Inc. (Docket B8/B8 C 1P)

Identification Reference by Depositor:

ATCC Designation

Escherichia coli M5219 (G-pPLA-HFIF-67-12deltaMI), HFIF-H

31824

Escherichia coli HB101 (p[325]-qHFIF-4), HFIF-I

31825

The deposits were accompanied by: ___ a scientific description X a proposed taxonomic description indicated above.

The deposits were received <u>February 26, 1981</u> by this International Depository Authority and have been accepted. A request to convert the deposits to a deposit under the Budapest Treaty was received on October 23, 1991.

AT YOUR REQUEST:

X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested October 25, 1991. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

Bobbie A. Brandon, Head, ATCC Patent Depository

Date: October 28, 1991

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDENT	TIFICATION OF THE MICROORGANISM	
Identifica	tion reference given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY
нвіс	01(G-pBR322(Pst)/HFIF 3)	DSM 1791
II. SCIEN	NTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGN.	ATION
(organism identified under I. above was accompanied by:) a scientific description X) a proposed taxonomic designation	•
(Mark wit	h a cross where applicable)	
III. RECE	IPT AND ACCEPTANCE	!
	national Depositary Authority accepts this microorganism i $81-10-01$ (Date of original deposit) ¹	dentified under I. above, which was received by it
IV. RECE	IPT OF REQUEST FOR CONVERSION	:
(date of or	organism identified under I above was received by this Interciginal deposit) and a request to convert the original deposit y it on 1991–10–24 (date of receipt of request fo	to a deposit under the Budapest Treaty was
V. INTER	NATIONAL DEPOSITARY AUTHORITY	
Name:	DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH	Signature(s) of person(s) having the power to represent the International Depositary Author::, or of authorized official(s):
Adress:	Mascheroder Weg 1 B D-3300 Braunschweig	Date: 1991-10-28

Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired Form DSM-BP/4 (sole page) 0291

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM	
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1791 Date of the deposit or of the transfer 1: 1981-10-01	
III. VIAB	ILITY STATEMENT	•	
On that d	The viability of the microorganism identified under II above was tested on 1989-07-07. On that date, the said microorganism was (X) ³ viable () ³ no longer viable (V. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴		
IV INTE	RNATIONAL DEPOSITARY AUTHORITY		
14. 1141 61	CONTROL DEPOSITARY AUTHORITY		
Name: Address:	DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): Date: 1991-10-28	

Form DSM-BP/9 (sole page) 0787

Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

Fill in if the information has been requested and if the results of the test were negative.

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-B	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY:
	DGW 1700
HB101(G-pBR322(Pst)/HFIF 6)	DSM 1792
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIG	NATION
The microorganism identified under I. above was accompanied by:	·
() a scientific description(X) a proposed taxonomic designation	
(Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism on 1981-10-01 (Date of original deposit) ¹	m identified under I. above, which was received by it
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this In (date of original deposit) and a request to convert the original deposit received by it on 1991-10-24 (date of receipt of request	osit to a deposit under the Budapest Treaty was
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN Gmb	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):
Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Date: 1991-10-28

Form DSM-BP/4 (sole page) 0291

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM	
Address: C	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts JSA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1792 Date of the deposit or of the transfer 1: 1981-10-01	
III. VIABILIT	Y STATEMENT	•	
On that date, (X	of the microorganism identified under II above was teste the said microorganism was) 3 viable) 3 no longer viable DNS UNDER WHICH THE VIABILITY TEST HAS BE		
IV. INTERNAT	TIONAL DEPOSITARY AUTHORITY		
MII Address: Ma	M DEUTSCHE SAMMLUNG VON KROORGANISMEN UND ZELLKULTUREN GmbH scheroder Weg 1 B 3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): Date: 1991-10-28	

Form DSM-BP/9 (sole page) 0787

Indicate the date of original deposition, where a new deposition a transfer has been made, the most recent relevant date (date of the new deposition date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

Fill in if the information has been requested and if the results of the test were negative.

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDENTIFICA	ATION OF THE MICROORGANISM	
Identification re	eference given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY:
	G-pBR322(Pst)/HFIF 7)	DSM 1793
II. SCIENTIFI	C DESCRIPTION AND/OR TAXONOMIC DESIGN.	ATION
The microorgan	ism identified under I. above was accompanied by:	·
) a scientific description) a proposed taxonomic designation	
(Mark with a cre	oss where applicable)	
III. RECEIPT A	ND ACCEPTANCE	
	al Depositary Authority accepts this microorganism i 10-01 (Date of original deposit)	dentified under I. above, which was received by it
IV. RECEIPT O	F REQUEST FOR CONVERSION	
(date of original	sm identified under I above was received by this Interdeposit) and a request to convert the original deposit 1991-10-24 (date of receipt of request for	·
V. INTERNATI	ONAL DEPOSITARY AUTHORITY	
	I-DEUTSCHE SAMMLUNG VON ROORGANISMEN UND ZELLKULTUREN GmbH	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):
	cheroder Weg 1 B 300 Braunschweig	Date: 1991-10-28

Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired Form DSM-BP/4 (sole page) 0291

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOS	SITOR	II. IDENTIFICATION OF THE MICROORGANISM	
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY. DSM 1793 Date of the deposit or of the transfer 1 1981-10-01	
III. VIAB	ILITY STATEMENT		
On that d	lity of the microorganism identified under II above was teste ate, the said microorganism was X) ³ viable 3 no longer viable OITIONS UNDER WHICH THE VIABILITY TEST HAS B		
IV. INTE	RNATIONAL DEPOSITARY AUTHORITY		
Name: Address:	DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): Date: 1991-10-28	

Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date; three in the new deposit or date of the transfer).

In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM			
Identification reference given by the DEPOSITOR HFIF-D	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY:		
M5219 (G-pPLa-HFIF-67-12)	DSM 1851		
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGN.	ATION		
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation			
(Mark with a cross where applicable)			
III. RECEIPT AND ACCEPTANCE			
This International Depositary Authority accepts this microorganism identified under I. above, which was received by it on 1981-10-01 (Date of original deposit) ¹			
IV. RECEIPT OF REQUEST FOR CONVERSION			
The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).			
V. INTERNATIONAL DEPOSITARY AUTHORITY			
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):		
Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Date: 1991-10-28		

Form DSM-BP/4 (sole page) 0291

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM		
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1851 Date of the deposit or of the transfer 1: 1981-10-01		
III. VIABI	LITY STATEMENT	·		
On that di	The viability of the microorganism identified under II above was tested on 1990-11-29. On that date, the said microorganism was (X) ³ viable () ³ no longer viable IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴			
IV. INTER	NATIONAL DEPOSITARY AUTHORITY			
Name: Address:	DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): Date: 1991-10-28		

Form DSM-BP/9 (sole page) 0787

Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date of the original deposit or date of the transfer).

In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viribility test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR HFIF-E	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY:
K12∆HI (G-pPLa-HFIF-67-12)	DSM 1852
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGN	ATION
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation	·
(Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism on 1981-10-01 (Date of original deposit) ¹	identified under I. above, which was received by it
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this Inter (date of original deposit) and a request to convert the original deposit received by it on 1991-10-24 (date of receipt of request for	to a deposit under the Budapest Treaty was
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):
Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Date: 1991-10-28

Form DSM-BP/4 (sole page) 0291

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquire.i

VIABILITY STATEMENT issued pursuant to Rule 10.2 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. DEPO	SITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1852 Date of the deposit or of the transfer 1: 1981-10-01
III. VIAB	ILITY STATEMENT	
On that d	ity of the microorganism identified under II above was testerate, the said microorganism was X) ³ viable 3 no longer viable ITIONS UNDER WHICH THE VIABILITY TEST HAS BE	
IV. INTER	NATIONAL DEPOSITARY AUTHORITY	
Name: Address:	DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): Date: 1991-10-28

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Indicate the date of original deposition, where a new deposition a transfer has been made, the most recent relevant date (late of the new deposition date of the transfer).

In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDEN	TIFICATION OF THE MICROORGANISM	
Identifica	ation reference given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY:
M52	19 (G-pPLa-HFIF-67-12∆19)	DSM 1853
II. SCIE	NTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGN	ATION
The micro	oorganism identified under I. above was accompanied by:	•
(a scientific description X) a proposed taxonomic designation	
(Mark wit	th a cross where applicable)	
III. RECE	CIPT AND ACCEPTANCE	
This Inter	rnational Depositary Authority accepts this microorganism $81-10-01$ (Date of original deposit) ¹	identified under I. above, which was received by it
IV. RECE	CIPT OF REQUEST FOR CONVERSION	
(date of o	porganism identified under I above was received by this Interriginal deposit) and a request to convert the original deposit by it on 1991–10–24 (date of receipt of request for	t to a deposit under the Budapest Treaty was
V. INTER	RNATIONAL DEPOSITARY AUTHORITY	
Name:	DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):
Adress:	Mascheroder Weg 1 B D-3300 Braunschweig	Date: 1991-10-28

Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired Form DSM-BP/4 (sole page) 0291

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOS	ITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1853 Date of the deposit or of the transfer 1: 1981-10-01
III. VIABII	LITY STATEMENT	·
On that da	ty of the microorganism identified under II above was tested. Ite, the said microorganism was X) ³ viable) ³ no longer viable TIONS UNDER WHICH THE VIABILITY TEST HAS BE	
IV. INTER	NATIONAL DEPOSITARY AUTHORITY	
	DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): Date: 1991-10-28

Form DSM-BP/9 (sole page) 0787

Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDEN	TIFICATION OF THE MICROORGANISM	
Identific HFI	ation reference given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY
M52	19 (G-pPlc-HFIF-67-8)	DSM 1854
II. SCIE	NTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGN	ATION
1	oorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation	
(Mark wi	th a cross where applicable)	
III. RECI	EIPT AND ACCEPTANCE	
This Inter	rnational Depositary Authority accepts this microorganism 81-10-01 (Date of original deposit) ¹	dentified under I. above, which was received by it
IV. RECE	CIPT OF REQUEST FOR CONVERSION	
(date of o	porganism identified under I above was received by this Interriginal deposit) and a request to convert the original deposit by it on 1991–10–24 (date of receipt of request for	to a deposit under the Budapest Treaty was
V. INTER	NATIONAL DEPOSITARY AUTHORITY	
Name:	DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):
Adress:	Mascheroder Weg 1 B D-3300 Braunschweig	Date: 1991-10-28

Form DSM-BP/4 (sole page) 0291

Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOS	ITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1854 Date of the deposit or of the transfer 1: 1981-10-01
III. VIABI	LITY STATEMENT	
On that da	ty of the microorganism identified under II above was teste te, the said microorganism was X) ³ viable) ³ no longer viable TIONS UNDER WHICH THE VIABILITY TEST HAS BE	
IV. INTER	NATIONAL DEPOSITARY AUTHORITY	
Address:	DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): Date: 1991-10-28

Indicate the date of original deposition, where a new deposition a transfer has been made, the most recent relevant date (date fine new deposition date of the transfer).

In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

PATENTS

Examiner

J. Martinell :

Group

1805

:

:

Applicant

Walter C. Fiers

Serial No.

387,503

Filed

July 28, 1989

For

DNA SEQUENCES, RECOMBINANT DNA MOLECULES AND PROCESSES FOR PRODUCING HUMAN FIBROBLAST

INTERFERON-LIKE POLYPEPTIDES

New York, New York June 3, 1994

DECLARATION OF JAMES F. HALEY, JR.

I, JAMES F. HALEY, JR., declare that:

- I am the attorney of record in the aboveidentified patent application. I make this declaration to set forth the facts related to the deposit of microorganisms referred to on pages 94-95 of that application and to the permanence, availability and replacement of those cultures.
- I identify the following documents that demonstrate the deposit of those microorganisms and the permanence, availability and replacement of those cultures:

Exhibit 1 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance", dated April 2, 1980 for deposit HFIF-A (DSM 1791); (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 2 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance", for culture HFIF-B (DSM 1792), dated April 2, 1980; (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 3 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance", dated April 2, 1980, for culture HFIF-C (DSM 1793); (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 4 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance" for culture HFIF-D (DSM 1851), dated June 5, 1980; (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 5 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance" for culture HFIF-E (DSM 1852), dated June 5, 1980; (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming

that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 6 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance" for culture HFIF-F (DSM 1853), dated June 5, 1980;
(b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit;
(c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit.

Exhibit 7 -- True copies of (a) Deutsche Sammlung von Mikroorganismen "Acknowledgement of Receipt and Acceptance" for culture HFIF-G (DSM 1854), dated June 5, 1980; (b) October 16, 1991 letter to the DSM with enclosures including a request to convert this deposit to a Budapest Treaty deposit; (c) Receipt of Request And Viability Statement from DSM confirming that this deposit has been converted to a Budapest Treaty deposit; (d) April 28, 1994 letter from DSM with enclosures including a revised Receipt of Request for this deposit.

Exhibit 8 -- True copies of (a) American Type Culture Collection "Acknowledgement of Receipt and Acceptance" for cultures HFIF-H and HFIF-I (ATCC 31824, ATCC 31825), dated February 27, 1981; (b) October 16, 1991 letter to ATCC with enclosures including a request to convert these deposits to Budapest Treaty deposits; (c) Receipt of Request And Viability Statement from ATCC confirming that these deposits have been converted to Budapest Treaty deposits; (d) revised Receipt of Request from ATCC for these deposits, dated May 6, 1994.

3. On the bases of the above-identified exhibits, I am informed and believe that the deposits of microorganisms referred to on pages 94-95 of the above-identified application were made, have been converted to deposits under the Budapest Treaty On The International Recognition Of The Deposit Of Microorganisms For The Purposes Of Patent Procedure, and are being maintained under the applicable rules and regulations of that Treaty and of the United States Patent and Trademark Office as to their permanence, availability and replacement.

- 4. On the basis of Exhibit 7, I am informed and believe that the deposit papers referring to deposit DSM 1854 have been amended. In the amended papers, deposit DSM 1854 refers to strain Escherichia coli HFIF-G M5219 (G-pPLc-HFIF-67-8). Attached as part of Exhibit 7 is an April 28, 1994 letter from Dr. Vera Weihs of the DSM explaining this amendment, along with a copy of the amended Receipt form.
- 5. On the basis of Exhibit 8, I am informed and believe that the deposit papers referring to ATCC 31824 and ATCC 31825 have been amended. In the amended papers, deposit ATCC 31824 refers to strain Escherichia coli M5219 (G-pPLa-HFIF-67-12AMI) and deposit ATCC 31825 refers to strain Escherichia coli HB101 (p[325]-gHFIF4). Attached as part of Exhibit 8 is a May 6, 1994 amended Receipt from ATCC.
- 6. I am informed and believe that the applicant agrees to maintain the permanence of these deposits for the full enforceable term of any patent issuing from this application and to irrevocably remove all restrictions on the availability to the public of the material so deposited upon granting of a patent.

7. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such wilful false statements may jeopardize the validity of this application or any patent issuing thereon.

JAMES F. HALEY, JR

Signed at New York, New York this 3rd day of June, 1994

GESELLSCHAFT FÜR BIOTECHNULOGISCHE FORSCHUNG MBH

DSM - Grisebachstrasse 8 - D-3400 Göttingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address of depositor:

Biogen N.V. 24 Handelskad

Willemsted Curacao, Netherland Antilles

Identification reference of

the microorganism used by the depositor:

HB101(G-pBR322(Pst)/HFIF 3)

Taxonomic designation of the microorganism provided by the depositor: Escherichia coli

DSM accession number of the microorganism: DSM 1791

Date of receipt of the viable microorganism:

April 2, 1980

In addition to the identification reference and the taxonomic designation the depositor has provided a scientific description of the microorganism.

The microorganism has been sent to the DSM directly by the depositor.

The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microoganism may be rendered accessible to any third party under the following conditions:

without any restrictions

according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or

according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning nr 12, 1979)

in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present form P 2570)

in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part

of the disclosure of the invention

in accordance with the French patent law

in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, April 2, 1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN

der

Gesettschaft für Biotechnologische Forschung mbH Gnaebachstraße 8

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.; (05.31) 70.08—1, Teles: 9—5.26.67

Vorsitzender des Aufsichtsrats: N. n. Dir. Dr. Friedrich Bischoff Geschättsführer: Dr. Maria Regina Kula Dr. Heimut Zeittfäger Bankkonto Gebr Löbbecke, Brautur (***) Konto 23 761 (BLZ (210) = 4 Registergericht: Amtwer ont Braunsor HRB 477 FISH & NEAV

B75 THIRD AVENUE NEW YORK, N.Y. 10022-6250

CHARLES SOITS DAVIOW OLAST ALBERT E PET JOHN O TRANSPORT

JANES F MALEY, JR RICHARDO M BARNES LAMBRUECE S MODERS TWOMAS L. BLALADINI MODERT J. BOLDMAN TWOMAS L. BECREST DANIEL M. BAMER REVINA CULLINAR

TELEPHONE, WIRL TISLOGOO TELEX 14-8367 CABLE ADDRESS: FISHNEAVE TELECOPIER: (212) 715-0674

October 16, 1991

----1889-1830 CHARLES MEAVE 1867-1937

> Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH Mascheroder Weg 1b D-3300 Braunschweig Federal Republic of Germany

> > Biogen - B8/B8 CIP Deposits DSM 1791-1793; 1851-1854

Dear Sir:

We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,

James F. Haley,

Ivor R. Elrifi

Attorneys for Biogen, Inc.

JFH/IRE:bb Enclosures

A PETER ABLES MICHARD A 1413

DUAMETERNID MOUS-MITCHELL M BEDOS JOHN F WARD JOHN F WARD DUAMED J DEFRANCO MANGE D BOWLAND MANGE D BOOKLAND DUAL MANGE DESK MANGE MISSAND DUIDA LOS WENTEN JOHN J CARRINGMAN JOHN J. CASSIMONN
LIGHT A WADLED
AGENETAL MIL
MARTA E DODGE
JOHN M. STORELLA
MILLAM J MCCASE
JOHN M. STORELLA
MILLAM J MCCASE
DOWN M. STORELLA
MILLAM J MCCASE
DOWN M. STORELA
MILLAM J MCCASE
JOHN M. SORMANA
MILLAM J MCCASE
JEFFRETH MEMO: MILLIAN A BEMOMERMY OF SHAP A MINGRO FORESTA WINDS FORESTOWNESS WARNESS WARRESTOWNESS WARNESS WARN

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT pursuant to Rule 6.1

FOR THE PURPOSE OF PATENT PROCEDURE

To DEUTSCHE SAMPLING VON MICROORGANISMEN UND ZELLKULTUREN GABH Mascherouer Meg 1b D-3300 Brownschweig Federal Republic of Germany

To	be	fi	lle	ø i	in t	ΟY	the	De	006	itar	7	Aut	חפר	ity	
1	09	4-A	æ	5 5 i	ion	nu	St.	r:							
1	Dat	te -	مال	tur	·e r	rec	:eiv	ed :	:						

BACTERIA/FLNGI

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROGREAMISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN BULE 9.1^2

Identification reference ³ :	The culture to be deposited is :		
HFIF-A	(X) a pure culture		
HB101(G~pBR322(Pst)/HFIF 3) (axonomic designation :	() a mixture of microorganisms		
Escherichia coli	(Mark with a cross where applicable)		
. CONDITIONS FOR CULTIVATION	(X) ⁵		
edium:	pH before sterilisation :		
as according to original	Sterilisation min at *C		
deposit application for DSM 1791	pH efter sterilisation:		
	Oxygen relationship :		
	() aerobic		
	() micromerophilic		
	() obligate anmerobic		
·	Specific gaseous requirements :		
	Incubation temperature: "C		
	Incubation time:		
	Short term storage at: *C		
	Interval of transfer:		

The DSM only accepts for deposit microorganisms which belong to hazard group 1 or 11, according to 01M 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. überarbeitete Fassung BMFT)

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the microorganism be indicated.

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/Fung: (first page) 0488

III. COMDITIONS FOR LONG TERM STORAGE,	(X) ⁵
	(x) ⁵
IV. CONDITIONS FOR TESTING VIABILITY	СХУ
	·
V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(X) ⁵
Description of components:	
ethod(s) for checking presence of components:	

5 Hark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGER. TO HEALTH OR ENVIRONMENT	
Mazard group of the microorganisms named under I. according to DIN 58 956 (Beiblatt 1) Teil 1, Medizinis Mikrobiologie, ISBN 3-410-12028-9:	che
THE STRAIN HAS TO BE MANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL 1:	
() 12	
() 13	
IS THIS STRAIN DANGEROUS TO REALTH OR THE ENVIRONMENT? (·) YES (X) NO	
(if yes, please specify:) (X) ⁵	
(X) the undersigned is not aware of such properties	
IF THE MICROORGANISM IS GENETICALLY MANIPULATED:	
1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:	
general genetic recombination (rec):	
sensitivities:	
resistances:	
modifications:	
restrictions:	
auxotrophies:	
2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF LMICH MAS BEEN CLONED INTO THE PLASMID:	
3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines ² or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE GUESTIONS THE ORGANISM CAMMOT BE ACCEPTED FOR DEPOSITION).	
1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY HAVE NO PATHOGENIC POTENTIAL.	
() TES	
2. THE SUBGENOMIC FRACMENTS HAVE A PATHOGENIC POTENTIAL.	
() YES	
IN THE LATTER CASE PLEASE NOTE:	
According to the regulations of the ZKBS ⁶ the DSM can only accept genetically magipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS ⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form	Y

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. überarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VII. SCIE	MIFIC DESCOH?	(x) ⁵
VIII. ADDI	TIONAL DATA	8ر ع
IX. DEPOSI	TOR ⁹	
	P 1	tales of
Hame:	Biogen, Inc.	Signature: L. BOW
		James F. Haley, Jr. Ivor R. Elrifi
		Attorneys for Biogen, Inc. Fish & Neave
Address:	<pre>14 Cambridge Center Cambridge, Massachusetts</pre>	
		10/18/91
		,

5 Mark with a cross if additional information is given on an attached sheet.

required.

there the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

Mark with a cross if additional information is given on an attached sheet.

It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.)

of the microorganism be indicated.

Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).

The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.

FOR THE PURPOSES OF PATENT PROCES

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY:
HFIF-A	new 1701
HB101(G-pBR322(Pst)/HFIF 3)	DSM 1791
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNA	TION
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation	
(Mark with a croes where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism i on 1981-10-01 (Date of original deposit) ¹	dentified under I. above, which was received by it
IV. RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this Inte (date of original deposit) and a request to convert the original deposit received by it on 1991-10-24 (date of receipt of request to	to a debout auger eine Dagabers ander,
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorised official(s):
Adrees: Mascheroder Weg 1 B D-3300 Braunschweig	Date: 1991-10-28

¹ Where Rule 6.4(d) applies, such date is the date on which the etatus of international depositary authority was acquired Form DSM-BP/4 (sole page) 0291

RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCED

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1791 Date of the deposit or of the transfer 1: 1981-10-01
III. VIABI	LITY STATEMENT	
On that do	ity of the microorganism identified under II above was teste ate, the said microorganism was X) ³ viable 3 no longer viable	ed on 1989-07-07 .2
(ITIONS UNDER WHICH THE VIABILITY TEST HAS B	EEN PERFORMED ⁴
IV. INTE	RNATIONAL DEPOSITARY AUTHORITY	

Form DSM-BP/9 (sole page) 0787

Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

Fill in if the information has been requested and if the results of the test were negative.

DSM - Grisebachstrasse 8 - D-3400 Göttingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address of depositor:

Biogen N.V. 24 Handelskad Willemsted

Curacao, Netherland Antilles

Identification reference of the microorganism used by the depositor:

HFIF-B

HB101(G-p8R322(Pst)/HFIF 6)

Taxonomic designation of the microorganism provided by the depositor:

Escherichia coli

DSM accession number of the microorganism;

DSM 1792

Date of receipt of the viable microorganism:

April 2, 1980

In addition to the identification reference and the taxonomic designation the depositor YYak ANOVAGENAY has not provided a scientific description of the microorganism.

In microorganism has been sent to the DSM directly by the depositor.

The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microoganism may be rendered accessible to any third party under the following conditions:

| | without any restrictions

according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSH (Official Journal EPO 5, 301-307, 1978) and/or

according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttidning or 12, 1979)

in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present form P 2570)

in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon grating of a United States patent wherein the deposited microorganism is part

of the disclosure of the invention [X] in accordance with the French patent law

in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, April 2, 1980

Place

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN Signature

der Gesellechaft für Biotechnologische Forschung mbH

Grisebachstraße 8

D-3400 Göttingen

Geselfschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tet.: (05.31) 70.08—1, Teles: 9—5.26.87

Vorsitzender des Aufsichtsrats: Min. Dir. Dr. Friedrich Bischoff

Geschättstührer: Dr. Maria Regina Kula Dr. Helmut Zeitiräger Bankkonto: Gebr. Löbbecke, Braunschweig Konto 23 781 (BLZ 270 305 CO) Registergericht: Amisgericht Brauns. HAB 477

FISH & NEAV

JAMES F MALEY, JR RICHARD M BARNES LAMENCE S ROGER FROMEN, BARNETT VINCENT M. BALLADIN ROSERT J. GOLDMAN THOMAS L. BECREST DANIEL M. BARTT MORMAS M. BEAMER

ID STATE OFFICER'S STATE OF THE
NEW YORK, N.Y. 10022-6250

TELEPHONE IZIZI 7:5-0600

TELEX 14-8367

CABLE ADDRESS: PISHNEAVE
TELECOPIER: (ZIZI 7:5-0674

-

SEISTIME MACEET
AREET JUDOOME
SERANDA DESIAD
MICHAEL P. DODRIS
JORNEW MATHEMY
DODRALDE SEED
ARMITES IN MALL
DOMALD A DESIAD
JENNIFES IN MALL
OCHAEL O SMOOND
SEIDON DE MENDO
LIAMMAC ALLEMP
SEADONDE PREDEN
MOSETS WILDES
CHIERONSES J MARSEY
MARIE IN MARIETI

A PETER ABLES SIGNARD A MIZ

DANTO C MLACRE
JAME A MASSAND
DUAME-BAYID MOUSE
MITCHELL R GROOM
JOHN F WARD
EDWARD J. DIFTRANCO
MASSAND GOWLAND
PULLIPREY F STEEL
MASSAND E MSELMANN
ESICH MUSBARD
DAVID P. LOWEMSTEIN
DAVID P. LOWEMSTEIN

SALE A SULPANDO DAVIDO LOÑ WENTE IN JOHN J. CARRINGMAN LINGUEZ CARRINGMAN LINGUEZ CARRINGMAN SULPAN E SUCOS JOHN W SINTZ JOHN W STORELLA WILLIAM J WEGARE JOHN W STORELLA WILLIAM J WEGARE VICEI D VECNERA LEBLIER A WEGARELLA LEBLIER A WEGARELLA LEBLIER A WEGARELLA LEBLIER A WEGARELLA

October 16, 1991

October 10

PREDERICK R FISH 1855-1830 CHARLES NEAVE 1867-1837

> Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH Mascheroder Weg lb D-3300 Braunschweig Federal Republic of Germany

> > Biogen - B8/B8 CIP Deposits DSM 1791-1793; 1851-1854

Dear Sir:

We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,

James F. Haley, Ivor R. Elrifi

Attorneys for Biogen, Inc.

JFH/IRE:bb Enclosures

RECOGNITION OF THE DEPOSIT OF HICKOR 1576 FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT pursuant to Rule 6.1

DEUTSCHE SAMULUNG VON MIKROORGANISMEN UND ZELLKULTUREN GRON Mescheroder Meg 1b D-3300 Braunschweig Federal Republic of Germany

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	09	1-A	œ	# \$	ion		er :	:						
	Dat	e	a	tu	re r	ece i	ve d	:						

BACTERIA/FUNGI

THE UNDERSIGNED HEREBY DEPOSITS LADER THE BUDDAPEST TREATY THE MICROORGANISM, IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO MITHORAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN BULE 9.12

1. IDENTIFICATION OF THE HICROORGANISM	
Identification reference ³ : HFIF-B HBl01(G-pBR322(Pst)/HFIF 6) Taxonomic designation ⁶ : Escherichia coli	The culture to be deposited is: (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
11. COMDITIONS FOR CULTIVATION	(x) ⁵
as according to original deposit application for DSM 1792	pH before sterilisation: Sterilisation min at *C pH after sterilisation: Oxygen relationship: () aerobic () microserophilic () obligate anserobic Specific gaseous requirements:
	Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:

form DSM-BP/1-Bacteria/fungi (first page) 0488

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIM 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the Laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte

Nukternsauren* (5. uberarbeitete Fassung BMFT)

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budgeost Treaty, with the same depositery institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of

international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronty recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the microorganism be indicated.

Mark with a cross if additional information is given on an attached sheet.

111. COMDITIONS FOR LONG TERM STORAGE	(x) ⁵
IV. CONDITIONS FOR TESTING VIABILITY	(x) ⁵
11. 00011100	<u> </u>
V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(x) ⁵
Description of components:	
Method(s) for checking presence of components:	

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DAL AGUS TO HEALTH OR ENVIRONMENT	
Mazard group of the microorganisms named under 1. according to DIN 58 956 (Beiblatt Mikrobiologie, ISBN 3-410-12028-9:	t 1) Teil 1, Medizinische
THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL 1:	
() 12	
() 13	
IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ? () YES	(_X) NO (X) ⁵
(if yes, please specify:)	(x) ⁻
(X) the undersigned is not aware of such properties	
IF THE MICROORGANISM IS GENETICALLY MANIPULATED:	
1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:	
general genetic recombination (rec):	
sensitivities:	
resistances:	•
modifications:	
restrictions:	
auxotrophies:	
2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE	PLASHID:
 If the strain is genetically manipulated the depositor must take appropriate sternathogenic potential (see: ZKBS guidelines) or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE GUESTIONS THE ORGANISH FOR DEPOSITION). 	
1. THE SUBGENOMIC FRACMENTS OF THE DNA DEFINETLY NAVE NO PATHOGENIC POTENTIAL.	
() YES	
2. THE SUBGENOMIC FRACMENTS HAVE A PATHOGENIC POTENTIAL.	
() YES	
IN THE LATTER CASE PLEASE NOTE:	
According to the regulations of the ZKBS ⁶ the DSM can only accept genetically meaningenic organisms for deposition when a copy of the permit issued by the ZKB valent national biological safety commission) for work on the organisms accompanisms	S (or by an equi-

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. uberarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

RECOGNITION OF THE DEPOSIT OF MICROARGANISMS FOR THE PURPOSES OF FATENT PRC URE

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

. IDENTIF	ICATION OF THE MICROORGANISM	
Identificatio	n reference given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY
HFIF-	В	
нв101	(G-pBR322(Pst)/HFIF 6)	DSM 1792
II. SCIENT	IFIC DESCRIPTION AND/OR TAXONOMIC DESIGNAT	rion
(rganism identified under I. above was accompanied by:) a scientific description X) a proposed taxonomic designation	
(Mark with	a cross where applicable)	
III. RECEI	PT AND ACCEPTANCE	
This Intern	ational Depositary Authority accepts this microorganism id 1-10-01 (Date of original deposit)	entified under I. above, which was received by it
IV. RECE	PT OF REQUEST FOR CONVERSION	
(date of or	organism identified under I above was received by this Inter- iginal deposit) and a request to convert the original deposit y it on 1991–10–24 (date of receipt of request fo	to a deposit direct the Design
V. INTER	NATIONAL DEPOSITARY AUTHORITY	
Name.	DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH	Signature(s) of person(s) having the power to represent the International Depositary Authorition of of authorised official(s):
Adress	Mascheroder Weg 1 B D-3300 Braunschweig	Date: 1991-10-28
l		and a second

Form DSM-BP/4 (sole page) 0291

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

RECOGNITION OF THE DEPOSIT OF MICROORS ANISMS FOR THE PURPOSES OF PATENT PROCE LE

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSIT	OR	II. IDENTIFICATION OF THE MICROORGANISM	
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1792 Date of the deposit or of the transfer 1. 1981-10-01	
II. VIABIL	ITY STATEMENT		
On that da	y of the microorganism identified under II above was tester, the said microorganism was X)3 viable 3 no longer viable		
V. CONDI	TIONS UNDER WHICH THE VIABILITY TEST HAS B	EEN FERT CIGALED	_
IV. INTER	NATIONAL DEPOSITARY AUTHORITY		

Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

3 Mark with a cross the applicable box.

Form DSM-BP/9 (sole page) 0787

⁴ Fill in if the information has been requested and if the results of the test were negative.

German Collection Microorganisms

GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH

DSM - Grisebachstrasse 8 - D-3400 Göttingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

below has been deposited with the Deutsche Sammlung von Mikro-
Biogen N.V. 24 Handelskad Willemsted Curacao, Netherland Antilles
HFIF-C HB101(G-pBR322(Pst)/HFIF 7)
Escherichia coli
DSM 1793
April 2, 1980
ation reference and the texonomic designation the depositor has a scientific description of the microorganism.
een sent to the DSM directly by the depositor.
meen aent to the DSM on behalf of the depositor by the following esignation and accession number given:
the microogenism may be rendered accessible to any third party
C and to the agreement between the European Patent Organization Journal EPO 5, 301-307, 1978) and/or
sh patent legislation and to the agreement between the Swedish ISM (Svensk Patenttidning nr 12, 1979)
"Declaration of Release" to be filed by the depositor with the ent Office (at present Form P 2570)
Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) tates Code, section 122 (35 U.S.C. 122) of the United States of any restriction on availability to the public of the culture ted States patent wherein the deposited microorganism is part the invention
French patent law
conditions as specified by the depositor on enclosed separate
. 1980
DEUTSCHE SAMMLUNG VON MIKROORGANESMENITS
der Gesellschaft für Biotechnologische Forschung mbH Grøebachstraße 8

D-3400 Göttingen Gesettschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05.31) 70.08—1, Telex: 9—9.25.67

Vorsitzender des Aufsichtsrats: Min. Dir. Dr. Friedrich Bischoff

Geschäftstührer:

Dr. Mana-Regina Kula Dr. Helmut Zeitträger

Bankkonto: Gebr. Löbbecke, Braunschweig Konto 23 781 (BLZ 270 305 00) Registergericht: Amtspericht Braun: HRB 477

FISH & NEA

CHARLES SHITM DAVID W PLANT ALBERTE FET JONN D YAMMONTINE WERSERY F SCHWART LARS I SULLESEID WILLIAM J. SILBRETH WILLIAM J. SILBRETH EMIC C WOSLOM

JAMES F MALEY, JR RICHARD W BARRES LAURENCES ROCEMS VIOMAS L GLAMBETTI VINCENT W BALLADINO ROSERT J. BOLDMAN THOMAS L. SECREST DANIEL W. SANTH WIDMASS W. SEAMEN DANIEL M. GANTY
NORMAN M. BLAMEN
REVIN J. CULLIDAN
BLENN A. OUSTERMOA
BLEAN SROOFF
MARQARET A. PIERRY
ROW E. BANULMAN
DOUGLAB J. GLIBERY
OCKNIEL I. DEMMA

875 THIRD AVENUE NEW YORK, N.Y. 10022-6250 TELEPHONE (212) 715-0600 TELEX 14-8367 CABLE ADDRESS: FISHNEAVE TELECOPIER (212) 715-0674

October 16, 1991

C.JOSEM LAUSHON II
LIBA E CRISTAL
EDWARD N KELLY
MARK N BLOOMSERG
ALAN D SNIVN
DAVID C PLACHE
JAME A MARKARO
JAME A MARKARO DAVID C PALENTS
JAME & MARRARO
DUAME-DAVID NOUSH
MITCHELL N BROOK
JOHN F WARD
EDWARD J. DEFRANCO
MARK D ROWLAND
TO THE FORMATO
MARKO EMELMANO PHILIPPET MEBEN MARKO EMELMANO EDWARD J. MARTA E GROSS

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MARTA E GROSS JOHN W. STORELLA WILLIAM J. MCCASE JOHN M. DESMARAIS VICKIS VEENEM LESLIEA MEDORELL CHRISTOPHER P. 600

A PETER ADLER

------AMENT JUDIOME SERVING METALE M DOMALD L SHABHOW ELIZASTH W ALDRIC CLAY B WILSON DERENDAL PANICH: JERENT LACK JAMES F BERSIM JEWITEW W ALL JEWITEW W AL SOMPTO ENTERMOA TELLBELM MEMBA MITTIWW & SCHOMEMON WEBLE - WEBNIELDY HOBELS - NUMBER HOBELS - NUMBER BESEV - SONLENDO TESEV - SONLENDO TIVMES - VITAN TIVMES - NUMBER NUMBER -
THOMAS J VETTER

----1855-1930 CHARLES REAVE 1867-1937

> Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH Mascheroder Weg 1b D-3300 Braunschweig Federal Republic of Germany

> > Biogen - B8/B8 CIP Deposits DSM 1791-1793; 1851-1854

Dear Sir:

We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,

James F. Haley, Ivor R. Elrifi

Attorneys for Biogen, Inc.

JFH/IRE:bb Enclosures

RECOGNITION OF THE DEPOSIT OF MICHOD FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT pursuant to Rule 6.1

DEUTSCHE SAMELUNG VON HIKROORGANISHEN UND ZELLICULTUREN GRON Mascheroder Weg 1b D-3300 Braunschweig Federal Republic of Germany

To be filled	in by the Depositary Authority
DSH-Access	sion number :
Date culti	re received :

BACTER LA/FUNGI

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGAMISM IDENTIFIED MEREUNDER AND UNDERTAKES NOT TO MITHORAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN BULE 9.12

1. IDENTIFICATION OF THE MICROORGANISM				
Identification reference ³ :	The culture to be deposited is :			
HFIF-C	(X) a pure culture			
HB101(G-pBR322(Pst)/HFIF 7) Taxonomic designation :	() a mixture of microorganisms			
Escherichia coli	(Mark with a cross where applicable)			
11. CONDITIONS FOR CULTIVATION	() ⁵			
Hedium:	ри before sterilisation :			
•	Sterilisation min at *C			
as according to original deposit application for	pH after sterilisation:			
DSM 1793	Oxygen relationship :			
	() merobic			
	() microaerophilic			
	() obligate anaerobic			
	Specific gaseous requirements :			
	Incubation temperature: *C			
	Incupation time:			
	Short term storage at: *C			
	Interval of transfer:			

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Hedizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte

Nukleinsauren" (5. uperarbeitete Fassung BMFT)

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of

intermational depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the microorganism be indicated.

Mark with a cross of additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/Fung: (first page) 0488

111. CONDITIONS FOR LONG TERM STORAGE	(x) ⁵
III. Capiticas vol. 1220	
	j
	(xo ⁵
IV. CONDITIONS FOR TESTING VIABILITY	
	;
THE PARTY OF THE P	(x) ⁵
V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	
Description of components:	
Description of components: Method(s) for checking presence of components:	

5 Mark with a cross if additional information is given on an attached sheet.

1	
VI. PROPERTIES EA. OUS TO HEALTH OR ENVIRONMENT	
Nazard group of the microorpanisms, named under I. according to DIN 58 956 (Beibl Mikrobiologie, ISBN 3-410-12028-9:	att 1) Teil 1, Medizinische
•••••	
THE STRAIN HAS TO BE NAMDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL 1:	
() L2	
() 14	
IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ? () YES	(X) NO
(if yes, please specify:)	(X) ⁵
(X) the undersigned is not aware of such properties :	
IF THE MICROORGANISM IS GENETICALLY MANIPULATED:	
1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:	
general genetic recombination (rec):	
sensitivities:	
resistances:	-
modifications:	
restrictions:	
auxotrophies:	
2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE	ME PLASMID:
 If the strain is genetically manipulated the depositor must take appropriate pathogenic potential (see: ZKBS guidelines) or equivalent national guidelines Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE GUESTIONS THE ORGAL FOR DEPOSITION). 	.)
1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY MAVE NO PATHOGENIC POTENTIAL	•
() YES	
2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.	
() YES	
IN THE LATTER CASE PLEASE NOTE:	
According to the regulations of the ZKBS ⁶ the DSM can only accept geneticall pathogenic organisms for deposition when a copy of the permit issued by the valent national biological safety commission) for work on the organisms acceptorm	ZKBS" (or by an equi-

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58056 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the (aboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. uberarbeitete fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

5 2KBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VII. 55	IENTIFIC DE.	PTION			(X),		<u> </u>
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111. A	DITIONAL DATA					()*		
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X. DEPC	SITOR ⁹						1	
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X. DEPC) //	dy	
C. DEPC	sıtox ⁹ Biogen,	Inc.		Signature:) //	de la	7
		Inc.			James I	F. Hal	ey, Jr.	
		Inc.			Ivor R.	. Elri	ey, Jr.	n, In
me:	Biogen,				Ivor R. Attorne Fish	. Elri eys fo & Nea	ey, Jr. fi r Bioge ve	n, In
me:	Biogen,	ridge Center			Ivor R. Attorne Fish 875 I	Elri eys fo & Nea hird	ey, Jr. fi r Bioge ve Avenue	
	Biogen,	ridge Center ge, Massachu			Ivor R. Attorne Fish 875 I	Elri eys fo & Nea hird	ey, Jr. fi r Bioge ve	
ne:	Biogen,	ridge Center ge, Massachu	setts		Ivor R. Attorne Fish 875 I	Elri eys fo & Nea hird	ey, Jr. fi r Bioge ve Avenue	

Mark with a cross if additional information is given on an attached sheet.

Hark with a cross if additional information is given on an attached sheet.

It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.

Bark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).

The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.

required. Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

FOR THE PURPOSES OF PATENT PROCEDU

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

entification reference given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY
HFIF-C HB101(G-pBR322(Pst)/HFIF 7)	DSM 1793
. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATI	ON
he microorganism identified under I. above was accompanied by: () a scientific description	
(X) a proposed taxonomic designation	
Mark with a cross where applicable)	
II. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism id on $1981-10-01$ (Date of original deposit) ¹	entified under $f 1$, above, which was received by it
on 1981-10-01 (Date of Original deposity	
IV. RECEIPT OF REQUEST FOR CONVERSION	
	national Depositary Authority on 1980–04–02 to a deposit under the Budapest Treaty was
IV. RECEIPT OF REQUEST FOR CONVERSION The microorganism identified under I above was received by this Inter (date of original deposit) and a request to convert the original deposit	national Depositary Authority on 1980–04–02 to a deposit under the Budapest Treaty was
IV. RECEIPT OF REQUEST FOR CONVERSION The microorganism identified under I above was received by this Inter (date of original deposit) and a request to convert the original deposit received by it on 1991-10-24 (date of receipt of request for	national Depositary Authority on 1980–04–02 to a deposit under the Budapest Treaty was

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired Form DSM-BP/4 (sole page) 0291

GNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

VIABILITY STATEMENT issued pursuant to Rule 10.2 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

		II. IDENTIFICATION OF THE MICROORGANISM
ddress:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1793 Date of the deposit or of the transfer 1 1981-10-01
i. VIABILI	TY STATEMENT	
The viability On that dat	y of the microorganism identified under II above was test e, the said microorganism was	
(X) ³ viable) ³ no longer viable	BEEN PERFORMED ⁴
(BEEN PERFORMED ⁴
()3 no longer viable	BEEN PERFORMED ⁴
IV. CONDI)3 no longer viable	
IV. CONDI) ³ no longer viable TIONS UNDER WHICH THE VIABILITY TEST HAS	Signature(s) of person(s) having the power

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new

Form DSM-BP/9 (sole page) 0787

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box. 4 Fill in if the information has been requested and if the results of the test were negative.

German Collection of Mi organisms

GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH

DSM - Grisebachstrasse 8 - D-3400 Göttingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

	ACKNOWLEDGEMENT	OF	RECEIPT	AND	ACCEPTANO	E
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ACKNOWLEDGERE	NI OF RECEIPT AND RECEIPT AND RECEIPT
The microorganism mentioned below has bee	n deposited with the Deutsche Sammlung von Mikro-
organismen.	BIOGEN N.V.
Name and address	24 Handelskad
of depositor:	Willemsted,
	Curacao, Netherland Antilles
Identification reference of	HFIF-D
the microorganism used by the depositor:	M5219 (G-pPLa-HFIF-67-12)
Taxonomic designation of	Escherichia coli
the microorganism provi- ded by the depositor:	
DSM accession number of	DSM 1851
the microorganism;	USN 1071
Date of receipt of the	June 5, 1980
viable microorganism:	
In addition to the identification referen	nce and the taxonomic designation the depositor NASX description of the microorganism.
The significant has been sent to t	the DSM directly by the depositor.
has been east to !	the DSM on behalf of the depositor by the following
depository under the designation and	d accession number given: -
under the following conditions: vition: Any restriction: according to Rule 28 EPC and to the and the DSM (Official Journal EPO 5 according to the Swedish patent leg. Patent Office and the DSM (Svensk P. in accordance with the "Declaration DSM and the German Patent Office (a in accordance with a) Title 37, Cod and Title 35, United States Code, s. X America and b) without any restrict upon granting of a United States pa of the disclosure of the invention	islation and to the agreement between the Securiti atentidning or 12, 1979) of Release" to be filed by the depositor with the t present Form P 2570) e of Federal Regulations, section 1.14 (37.CFR 1.14) ection 122 (35 U.S.C. 122) of the United States of ion on availability to the public of the culture itent wherein the deposited microorganism is part
	~ Comic
Göttingen, June 5, 1980	· D. Collins
DEUTSCHE 9	AMMILING VON MICROORGAMENTS
Place date	der at für Biotechnologische Forschung möhl
Geselischi	gr für Biotechnologische Polisialising morn. Geweinstrieße B

D-3400 Gottingen

Gesellschaft für Biotechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05.31) 70.08—1, Telez: 9—5.25.67

Vorsitzender des Aufsichtsrats: Min. Dir. Dr. Friedrich Bischoff

Geschättsführer: Dr. Mana-Regina Kula Dr. Helmul Zeitträger

Bankkonto: Gebr. Löbbecke, Braunschwerg Konto 23 781 (BLZ 270 305 00)

Registergericht: Amrsgenicht Brae HRB 477

The microorganism mentioned below is to be deposited with the DSM on account of a patent application (to be) filed with The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation (delete, if not applicable) Name and address of depositor: BIOGEN N.V. 24 Handelskad Willemsted Curacao, Netherland Antilles Identification reference of the microorganism given by the depositor (strain number, symbols etc.): HFIF - D M5219 (G-PPLa-HFIF-67-12) Taxonomic designation of the microorganism: A scientific description of the microorganism is attached on a separate sheet: YES [NO X The microorganism to be deposited is YES X a pure culture a mixture of strains : YES T NO In case of a mixed culture, please give a concise description on a separate sheet-about the components and methods to determine their viability. Does the microorganism and/or ist metabolic products present any hazard for man, animals, plants or the environment: (if any, please specify on a separate sheet): YES The microorganism will be east to the DSM directly by the depositor. The microorganism will be sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given: The microorganism may be rendered accessible after receipt and deposition to any third party without any restriction according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or according to the Swedish patent legislation and to the agreement between the Swedish Patent Dffice and the DSM (Swensk Patenttioning nr 12, 1979) in accordance with the "Declaration of Release" to be filed by the depositor with the in accordance with the "Declaration of nestage to of , DSM and the German Patent Office (at present Form 2750) in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14) and Title 35, United States Code section 122 (35 U.S.C. 122) of the United States of America and b) without any restrictions on the availability to the public of the culture upon granting of the United States patent wherein the deposited microorganism is parts.

1 for

deposition of patent microorganisms '

of the disclosure of the invention in accordance with the French patent law

sheet.

ACCESSION

DSM ISEI

DS/1 acc ion number:

Date culture received: 5 Julia 610

FISH & NEAVE

THOMAS J VETTER

CPAS MITSON

ETIESELM TOURIDE

ETIESELM TOURIDE

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TEMMILES WATTON

DOUTTO F GESTA

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VICTOR WEENER
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CHARLES S DAITY
DAVIDW PLANT
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HILLIAM J. BLESST
EDICC WORLDW
JOHNS E MATMAN
HOWELT C. WORSON
HOWELT
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HOWELT
JESSEL J. JENNEY
W ESPHARD RAILET
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JAMES? MALEY, AN BICHARD IN BARNES LAUBENCES BOOSEM YHOMAS, LOAD MAN BOOSEM YHOMAS, LOAD MAN BECKEST NORMAS, LOAD MAN BECKEST NORMAS, LOAD MAN BECKEST NORMAS L. BECKEST NORMAS IN BENTAL MINISTER NORMAS AND BENTAL MINISTER NORMAS AND BENTAL MINISTER NORMAS AND BENTAL MINISTER NORMAS IN BANKET NORMAS L. LOZITHO DENDAL L. LOZITHO DENDAL L. LOZITHO DEFENCY MINISTER NEW MAN BANKET NEW BENTAL L. LOZITHO DEFENCY MINISTER NEW BENTAL MAN BENTAL L. LOZITHO DEFENCY MINISTER NEW BENTAL MAN BENTAL L. LOZITHO DEFENCY MINISTER NEW BENTAL MINISTER NEW B

NEW YORK, N.Y. 10022-6250

TELEPHONE (ZIZI 715-0600

TELEX 14-8367

CABLE ADDRESS: PIBMNEAVE
TELECOPIER (ZIZI 715-0674

October 16, 1991

FREDERICK P. FIRM 1858-1830 CHARLES WEAVE 1867-1837

> Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH Mascheroder Weg lb D-3300 Braunschweig Federal Republic of Germany

> > Biogen - B8/B8 CIP Deposits DSM 1791-1793; 1851-1854

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Thanks for your help.

Yours very truly,

James F. Haley, Ivor R. Elrifi

Attorneys for Biogen, Inc.

JFH/IRE:bb Enclosures

RECOGNITION OF THE DEPOSIT OF MICROSRGA FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT pursuant to Rule 6.1

DEUTSCHE SAMPLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GOTON Mascheroder Weg 1b D-3300 Braumschweig Federal Republic of Germany

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	D 9	4-A	œ	esi	i i ar	-	, mbe	r:						
	Dat	te	a	lti	T.	rec	æiv.	ed:						

BACTERIA/FUNGI

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN MULE 9.1^2

1. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-D M5219 (G-pPLa-HFIF-67-12) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is: (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
11. COMPITIONS FOR CULTIVATION	(x) ⁵
Medium: as according to original deposit application for DSM 1851	pH before sterilisation: Sterilisation min at *C pH after sterilisation: Oxygen relationship: () serobic () microserophilic () obligate anserobic Specific gaseous requirements:
	Incubation temperature: *C
	Short term storage at: *C Interval of transfer:

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the microorganism be indicated.

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/fungi (first page) 0488

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIM 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Hukleinsauren" (5. uberarbeitete Fassung BMFT)

III. COMDITIONS FOR LONG TERM STORAGE +	(x) ⁵
	(X) ⁵
IV. CONDITIONS FOR TESTING VIABILITY	
THE COUNTY AND COUNTY AND COUNTY AND COUNTY	(X) ⁵
V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(x) ⁵
	(x) ⁵
	(x) ⁵
	(x) ⁵
	(x) ⁵
	(X) ⁵
	(x) ⁵
Description of components:	(x) ⁵
Description of components:	(x) ⁵
Description of components:	(x) ⁵
Description of components:	(x) ⁵
Description of components:	(x) ⁵
Description of components:	(x) ⁵
Description of components:	(x) ⁵
Description of components:	(x) ⁵
V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE) Description of components: Method(s) for checking presence of components:	(x) ⁵
Description of components:	(x) ⁵

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH O	RENVIRONMENT		
Hazard group of the microorganisms, Mikrobiologie, ISBN 3-410-12028-9:1	named under 1. according to DII	y 58 956 (Beiblatt	1) Teil 1, Medizinische
THE STRAIN HAS TO BE MANDLED UNDER 1	THE FOLLOWING LABORATORY CONTAI	IMMENT LEVEL 1:	
() 11	() 12		
() 13	() 14		
IS THIS STRAIN DANGEROUS TO MEALTH ((if yes, please specify:)	OR THE ENVIRONMENT ?	() YES	(X) мо (X) ⁵
			·
(X) the undersigned is not ass	are of such properties		
IF THE MICROCREANISM IS GENETICALLY	MANI PULATED:		
1. PLEASE INDICATE ALL THE RELEVANT	GENETIC PROPERTIES:		
general genetic recombination (re	ec):		
sensitivities:			
resistances:			
modifications:			
restrictions:			
auxotrophies:			
2. DESIGNATION OF THE DOMOR ORGANISM	K(S), THE ONA OF WHICH MAS BEEN	CLONED INTO THE	PLASMID:
3. If the strain is genetically manipathogenic potential (see: ZKBS please specify whether (WITHOUT AFOR DEPOSITION).	midalisas" or amulvalent natio	mai guideilnes.)	
1. THE SUBGENOMIC FRAGMENTS OF TO	HE DNA DEFINETLY HAVE NO PATHOX	ENIC POTENTIAL.	
() YES .			
2. THE SUBGENOMIC FRAGMENTS HAVE	A PATHOGENIC POTENTIAL.		
() YES			
IN THE LATTER CASE PLEASE NOTE:			
According to the regulations of pathogenic organisms for deposivatent national biological safe form	tion when a copy of the permit ty commission) for work on the	organisms accompl	nies the deposition
The DSM only accepts for deposit	microorganisms which belong to	hazard group I of	II, according to DIN

The DSM only accepts for deposit microorganisms with a cost of the property of

/II. SCI E	ENTIFIC DESCRIPTION?	(x) ⁵
		()8
11. ADC	DITIONAL DATA	()°
C. DEPOS	SITOR ⁹	
C. DEPOS	SITOR ⁹	J-g. Later of
		Signature: Jan J. Girl
	Biogen, Inc.	
		James F. Haley, Jr. Ivor R. Elrifi
me:	Biogen, Inc. 14 Cambridge Center	James F. Haley, Jr. Ivor R. Elrifi Attorneys for Biogen, In Fish & Neave
x. DEPOS	Biogen, Inc.	James F. Haley, Jr. Ivor R. Elrifi Attorneys for Biogen, In
ane:	Biogen, Inc. 14 Cambridge Center Cambridge, Massachusetts	James F. Haley, Jr. Ivor R. Elrifi Attorneys for Biogen, In Fish & Neave 875 Third Avenue

Mark with a cross if additional information is given on an attached sheet.

It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated.

or the microorganism be indicated.

Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositery institution(s) with which the microorganism has been deposited, or the criterion used when depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is <u>optional</u>). The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

RECOG! ON OF THE DEPOSIT FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

DENTIFICATION	ON OF THE MICROORGANISM	
	ence given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY
HFIF-D	-pPLa-HFIF-67-12)	DSM 1851
SCIENTIFIC	DESCRIPTION AND/OR TAXONOMIC DESIGNAT	ion .
he microorganii	im identified under I. above was accompanied by:	
	a scientific description a proposed taxonomic designation	
(Mark with a cr	oss where applicable)	
	and Acceptance onal Depositary Authority accepts this microorganism -10-01 (Date of original deposit) ¹	identified under ${f I}.$ above, which was received by it
IV. RECEIPT	OF REQUEST FOR CONVERSION	constional Depositary Authority on 1980-06-05
The microorg	t on 1991-10-24 (date of receipt of reques	ternational Depositary Authority on 1980–06–05 sit to a deposit under the Budapest Treaty was for conversion).
received by 1	ATIONAL DEPOSITARY AUTHORITY	
received by 1	ATIONADO	
v. INTERN	DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN Gm	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):

Form DSM-BP/4 (sole page) 0291

Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

TITION OF THE DEPOSIT OF MICROSIA FOR THE PURPOSES OF PATENT PROCEDURE ·REC

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

VIABILITY STATEMENT issued pursuant to Rule 10.2 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

DEPOSIT	DR .	II. IDENTIFICATION OF THE MICROORGANISM
	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1851 Date of the deposit or of the transfer 1. 1981-10-01
VIABIL	ITY STATEMENT	
on that da	y of the microorganism identified under II above was test te, the said microorganism was ×) ³ viable	ed on 1990-11-29 ²
•)3 no longer viable ITIONS UNDER WHICH THE VIABILITY TEST HAS !	BEEN PERFORMED ⁴
IV. COND	TIONS ONDER WILLIAM	
IV. INTE	RNATIONAL DEPOSITARY AUTHORITY	
IV. INTE	RNATIONAL DEPOSITARY AUTHORITY DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN Gmb	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):

¹ Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH

DSM - Grisebachstrasse 8 - D 3400 Gottingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen. BIOGEN N.V. Name and address 24 Handelskad of depositor: Willemsted, Curacao, Netherland Antilles HFIF-E Identification reference of the microorganism used by K124HI (G-pPLa-HFIF-67-12) the depositor: Taxonomic designation of Escherichia coli the microorganism provided by the depositor: DSM accession number of DSN 1852 the microorganism; Date of receipt of the June 5, 1980 viable microorganism: In addition to the identification reference and the taxonomic designation the depositor was provided / has not provided a scientific description of the microorganism. The microorganism has been sent to the DSM directly by the depositor. The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given: As stated by the depositor the microoganism may be rendered accessible to any third party under the following conditions: | | uithout any restrictions according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Swensk Patenttidning nr 12, 1979) in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570) in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the disclosure of the invention in accordance with the french patent law in accordance with the conditions as specified by the depositor on enclosed separate sheet. Göttingen, June 5,1980 DELITECHE SAMMLLING VON MIKROORGANISMEN Signature Place date der ichaft für Biotechnologische Forschung mbH

Gesellschaft für Biolechnologische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05.31) 70.08-1, Telex: 9-5.26.67

Vorsitzender des Aufsichtsrats: Min, Dir, Dr. Friedrich Bischoff

Geschättsführer:

Graebachetrate 8 D-3400 Göttingen

Konto 23 781 (BLZ 270 305 00)

Registergericht: HRB 477

Bankkonto:

(Permit Policerias of sectionidas

ACCESSION FORM: For

DSM accession number: DSM 1852

Date culture received: 5 Jane deposition of patent microorganisms The microorganism mentioned below is to be deposited with the DSM on account of a patent application (to be) filed with The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation (delete, if not applicable) BIOGEN N. V. Name and address of depositor: 24 Handelskad Willemsted Curacao, Netherland Antilles Identification reference of the sitor (strain number, symbols etc.): K120HI (G-pPLa- HFIF-67-12) Taxonomic designation of the microorganism: زامه .E A scientific description of the microorganism is attached on a separate sheet: YES 🔲 The microorganism to be deposited is a pure culture a mixture of strains : In case of a mixed culture, please give a concise description on a separate sheet-about the components and methods to determine their viability. Does the microorganism and/or ist metabolic products present any hazard for man, animals, plants or the environment: (if any, please specify on a separate sheet): YES 🔲 hand delivered

The microorganism will be seem to the DSH directly by the depositor. The microorganism will be sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given: The microorganism may be rendered accessible after receipt and deposition to any third party without any restriction according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Svensk Patenttioning or 12, 1979) in accordance with the "Declaration of Release" to be filed by the depositor with the DSH and the German Patent Office (at present Form 2750) in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14) and Title 35, United States Code section 122 (35 U.S.C. 122) of the United States of America and b) without any restrictions on the availability to the public of the culture upon granting of the United States patent wherein the deposited microorganism is part.4. of the disclosure of the invention in accordance with the French patent law

in accordance with the conditions as specified by the depositor on enclosed separate -

(Please mark what applies)

sneet.

FISH & NEAVE

THARLES & SHITH

DAVIDUS SLAMT

MAGEST (F ST

JOHN D VARSDAYNE

HERES SAN LASSE

FRILLIAM J SAN LASSE

FRILLIA

JAMERY MALEY, JOB RICHARDS IN BARNES LAUMENCES RODICES VINCERT IN BALLADHISTY VINCERT IN BALLADHISTY VINCERT IN BALLADHISTY MONDAL IN BALMAN MONDAL IN BANKE REVINA J. CULLINGAN BLEWIN A. DUSTER-WOLF BURNAN BRODDET MANDARET A. PIECE BONDAL IN J. CHEER DOUGHAR J. OLIBERT DE WISE L. LIDHING JEFFREY IN BALBARET
NEW YORK, N.Y. 10022-6250

TELEPHONE: 12121 719-0600

TELEX 14-8367

CABLE ADDRESS: PISHNEAVE
TELECOPIER: 12121 715-0674

October 16, 1991

FREDERICK P. FISH 1855-1830 CHARLES NEAVE 1887-1837

> Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH Mascheroder Weg lb D-3300 Braunschweig Federal Republic of Germany

> > Biogen - B8/B8 CIP Deposits DSM 1791-1793; 1851-1854

Dear Sir:

We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,

James F. Haley, Ivor R. Elrifi

Attorneys for Biogen, Inc.

'JFH/IRE:bb Enclosures SLOAGE MILE

C. JOSE DE LAMBORO...

INDRÉ CRISTAL

EDWARD " RELLY

RAMBOR D. LOCHERE

JAME D. BRITH

JAME A. MARANDO

ROMANDO " CALCHE

JOHNE D. CONCRET

ROMANDO " CONCRET

ROMAN

DEIELA

MINITIME RECORD THAN

WILLIAMS A SCHOOL THAN

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WICHAEL WILDON

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RECOGNITION OF THE DEPOSIT OF MICRODRIGA FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT pursuant to Rule 6.1

DEUTSCHE SAMULING VON HIKKOORGANISHEN UND ZELLEULTUREN GODN Mescheroder Weg 1b D-3300 Braunschweig Federal Republic of Germany

10	De	fi	11	€	in	Dγ	the	D) e	:00	6 I T	ar	y 4	wtt	or	lty	,	
	09	4-A	œ	es:	ian	n.	noe	٢	:									
	Dat		a	itL	re	rec	eiv	•	1	:								

BACTERIA/FUNGI

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDDAPEST TREATY THE MICROORGANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN BULE 9.12

1. IDENTIFICATION OF THE MICROORGANISM		
Identification reference ³ :	The culture to be deposited is :	
HFIF-E Kl2ΔHI (G-pPLa-HFIF-67-12)	(X) a pure culture() a mixture of microorganisms(Mark with a cross where applicable)	
Taxonomic designation :		
Escherichia coli		
II. COMDITIONS FOR CULTIVATION	(x) ⁵	
Hedium:	pH before sterilisation :	
	Sterilisation min at °C	
as according to original	pM after sterilisation:	
deposit application for DSM 1852	Oxygen relationship:	
53 5 3	() merobic	
	() microeerophilic	
	() obligate anaerobic	
	Specific gaseous requirements :	
	Incubation temperature: *C	
	Incubation time:	
	Short term storage at: °C	
	Interval of transfer:	

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIM 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte

² Containment level Li or L2 according to "Rightlinen zum schutz vor Gefanten Gurch in vitro neukombinierte kukleinsauren" (5. überarbeitete Fassung BMFT)
This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the microorganism be indicated.

⁵ Mark with a cross if additional information is given on an attached sheet.

TOWN STONE S	(x) ⁵
III. CONDITIONS FOR LONG TERM STORAGE	
	(×3 ⁵
IV. CONDITIONS FOR TESTING VIABILITY	(X2) .
	(x) ⁵
THE CONTRACT CONTRACT CONTRACT IN	(X)
V. COMPONENTS OF MIXED CULTURES (LIMEN APPLICABLE)	(X)
	(x)
	(*)
	(x)
V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE) Description of components:	(*)
	(*)
	(*)
Description of components:	
Description of components:	

5 Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH OR ENVIRONMENT		
Hazard group of the microorganisms named under 1. according to DIM 58 956 (Baiblatt 1) Teil 1, Medizinische Mikropiologie, ISBN 3-410-12028-9:		
THE STRAIN HAS TO BE NANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL 1:		
() 12		
() 13		
IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT? () YES (\times) NO (if yes, please specify:)		
(\mathbf{X}^{-}) the undersigned is not aware of such properties		
IF THE MICROORGANISM IS GENETICALLY MANIPULATED:		
1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:		
general genetic recombination (rec):		
sensitivities:		
resistances:		
modifications:		
restrictions:		
auxotrophies:		
2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:		
3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).		
1. THE SUBGENOMIC FRAGMENTS OF THE DWA DEFINETLY HAVE NO PATHOGENIC POTENTIAL.		
() YES		
2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.		
() YES		
IN THE LATTER CASE PLEASE NOTE:		
According to the regulations of the ZKBS ⁶ the DSM can only accept genetically manipulated, por pathogenic organisms for deposition when a copy of the permit issued by the ZKBS ⁶ (or by an example of the permit issued by the permit iss		

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment Level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. uberarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

VII. SCIE	NTIFIC DESCRIPTION	(x) ⁵
/III ADD	ITIONAL DATA	, B
X. DEPOS	ITOR ⁹	
X. DEPOS	Biogen, Inc.	James F. Haley, Jr. Ivor R. Elrifi Attorneys for Biogen, In-

Mark with a cross if additional information is given on an attached sheet.

It is strongly recommended that the scientific description and/or proposed taxonomic designation (see 1.) of the microorganism be indicated. of the microorganism be indicated.

Hark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depository institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).

The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.

required.

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

FOR THE PURPOSES OF PATENT PROC JURE

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM		
Identification reference given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY	
HFIF-E	DOM 1052	
K12AHI (G-pPLa-HFIF-67-12) DSM 1852		
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNATION		
The microorganism identified under I. above was accompanied by: () a scientific description	· 	
() a scientific description (X) a proposed taxonomic designation		
(Mark with a cross where applicable)		
III. RECEIPT AND ACCEPTANCE		
This International Depositary Authority accepts this microorganism i on 1981-10-01 (Date of original deposit) ¹	dentified under I. above, which was received by it	
IV. RECEIPT OF REQUEST FOR CONVERSION		
The microorganism identified under I above was received by this Inte (date of original deposit) and a request to convert the original deposit received by it on 1991-10-24 (date of receipt of request for	to a deposit under the Dadapar	
V. INTERNATIONAL DEPOSITARY AUTHORITY		
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH	Signature(z) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):	
Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Date: 1991-10-28	

Form DSM-BP/4 (sole page) 0291

¹ Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

FOR THE PURPOSES OF PATENT PROCED.

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

VIABILITY STATEMENT
ISSUED pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

I. DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM	
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1852 Date of the deposit or of the transfer 1: 1981-10-01	
III. VIABI	ILITY STATEMENT		
On that d	The viability of the microorganism identified under II above was tested on 1990-11-29 2 On that date, the said microorganism was (X) ³ viable () ³ no longer viable IV. CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED ⁴		
IV. INTE	RNATIONAL DEPOSITARY AUTHORITY		
Name: Address:	DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): Date: 1991-10-28	

Form DSM-BP/9 (sole page) 0787

lndicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

JEUTSCHE SAMMLUNG I N MIKKUUNGANISMEN

German Collection of Microorganisms GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH

DSM - Grisebachstrasse 8 - D-3400 Göttingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

HFIF-F

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Hikro-

Name and address of depositor:

BICGEN N.V. 24 Handelskad

Willemsted,

Curacao, Netherland Antilles

M5219 (G-pPLa -HFIF-67-12419)

Identification reference of the microorganism used by

the depositor:

Taxonomic designation of the microorganism provided by the depositor:

DSM accession number of the microorganism:

Date of receipt of the viable microorganism:

Escherichia coli

DSM 1853

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositorXMAX provided / has not provided a scientific description of the microorganism.

 $oldsymbol{ol}}}}}}}}}}}}}}}}}}}}}}}}$

O The microorganism has been sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microoganism may be rendered accessible to any third party under the following conditions:

O without any restrictions

according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO $\underline{5}$, 301-307, 1978) and/or

according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Swemsk Patenttidning or 12, 1979)

in accordance with the "Declaration of Release" to be filed by the depositor with the

OSN and the German Patent Office (at present form P 2570)

in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part of the displacement of the importance. of the disclosure of the invention

in accordance with the French patent law

in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5,1980

Place

DEUTSCHE SAMMLUNG VON MIKROORGANSMENSHature

der Gesellechalt für Biotechnologische Forschung mbM

Grischachatrade 8 D-3400 Göttingen

Gesellschaft für Biotechnotogische Forschung mbH, Mascheroder Weg 1, 3300 Braunschweig, Tel.; (05.31) 70.08—1, Telex: 9—5.26.87

Vorsitzender des Aufsichtsrats: Min. Dir. Dr. Friedrich Bischoff

Geschältsführer Dr. Maria-Regina Kula Dr. Helmut Zeilträger Bankkonto: Gebr. Löbbecke, Braunschweig Konto 23 781 (BLZ 270 305 00)

Registergencht: Amisgeneht Braunschweig HRB 477 ACCESSION FORM for DSH accession number: DSM 1553 deposition of patent microorganisms Date culture received: 5501015

The microorganism mentioned below is to be deposited with the DS4 on account of a patent application (to be) filed with

The deposit is made in accordance with Rule 28 EPC / with the Swedish patent legislation (delete, if not applicable) Name and address of depositor: BIOGEN N.V. 24 Handelskad Willemsted Curacao, Netherland Antilles Identification reference of the microorganism given by the depomicroorganism given by the depo-sitor (strain number, symbols etc.): HFIF - F M5219 (6- pPLa - HFJF -67-12 019) Taxonomic designation of the microorganism: A scientific description of the microorganism is attached on a meparate sheet: YES | The microorganism to be deposited is a pure culture a mixture of strains : In case of a mixed culture, please give a concise description on a separate sheet-about the components and methods to determine their viability. Does the microorganism and/or ist metabolic products present any hazard for man, animals, plants or the environment: (if any, please specify on a separate sheet): YES 🗌 120 XI Ine microorganism will be est to the DSH directly by the depositor. The microorganism will be sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given: The microorganism may be rendered accessible after receipt and deposition to any third party without any restriction according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSM (Official Journal EPO 5, 301-307, 1978) and/or according to the Swedish patent logislation and to the agreement between the Swedish Patent Office and the DSM (Swensk Patentioning or 12, 1979) in accordance with the "Declaration of Release" to be filed by the depositor with the DSH and the German Patent Office (at present Form 2750) in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14) and Title 35, United States Code aection 122 (35 U.S.C. 122) of the United States of America and b) without any reatrictions on the availability to the public of the culture upon granting of the United States patent wherein the deposited microorganism is party of the disclosure of the invention in accordance with the French patent law in accordance with the conditions as specified by the depositor on enclosed separate ...

FISH & NEAVE

875 THIRD AVENUE

NEW YORK, N.Y. 10022-6250

TELEPHONE. (212) 715-0600 TELEX: 14-0367 ----

JOHN F WARD
EDWARD, DEFRANCO
AMERICA DESCRIPTION
ONLINE DESCRIPTION
ONLINE DESCRIPTION
ONLINE DESCRIPTION
ENCO IN UNBARD
ENCO

MANTA E. GROSS
JOHN M. RIDTE
JOHN R. STORELLA
WILLIAM J. MCCASE
JOHN M. DESMARAIS
VICHIS VEENKER
LESLIE A MCDONELL
CHRISTOPHER P. 800

CABLE ADDRESS: FISHNEAVE TELECOPIES: (212) 715-0674

October 16, 1991

PREDERICK P FISH 1895-1830 CHARLES MEAVE 1967-1937

> Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH Mascheroder Weg lb D-3300 Braunschweig Federal Republic of Germany

> > Biogen - B8/B8 CIP Deposits DSM 1791-1793; 1851-1854

Dear Sir:

JAMES F MALEY, JR RICHARD IN BARNES LANGUAGE B BOOCHES THOMAS L. BARNESTI VINCENT IN BALLADISS BOSENT J. BOLDMAN THOMAS L. SECREST DANIEL IN BARTT DANIEL IN BARTT

We have enclosed seven (7) applications to convert the above-identified deposits already deposited at the DSM into deposits under the Budapest Treaty. The DSM designations, as well as the strain designations given by the depositor, are identified on the application forms. In addition, we enclose copies of the "Acknowledgement of Receipt and Acceptance" forms for these deposits and the "Accession Form for Deposit" for DSM 1851-1854, containing the media and culture requirements. Please send your debit note for these conversions to my attention.

Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,

James F. Haley, / Ivor R. Elrifi

Attorneys for Biogen, Inc.

'JFH/IRE:bb Enclosures BLDAPEST TREATY ON THE INTERNATIONAL

RECOGNITION OF THE DEPOSIT OF MICROORGANISPL

FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT pursuant to Rule 6.1

DEUTSCHE SAMULUNG VON MIKROORGANISMEN UND ZELLKULTUREN GRIDH Mascheroder Weg 1b D-3300 Braunschweig Federal Republic of Germany

		_
T	be filled in by the Depositary Authority	
	DSN-Accession number :	
	Date culture received :	

BACTERIA/FUNGI

THE UNDERSIGNED HEREBT DEPOSITS UNDER THE BUDAPEST TREATY THE MICROORGANISH IDENTIFIED HERELMDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN BULE 9.1^2

1. IDENTIFICATION OF THE MICROORGANISM	
Identification reference ³ : HFIF-F M5219 (G-pPLa-HFIF-67-12Δ19) Taxonomic designation ⁴ :	The culture to be deposited is: (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)
Escherichia coli	
11. CONDITIONS FOR CULTIVATION	(x) ⁵
Medium: as according to original deposit application DSM 1853	pH before sterilisation: Sterilisation min at *C pH after sterilisation: Oxygen relationship: () aerobic () microaerophilic
·	() obligate anaerobic Specific gaseous requirements:
	Incubation temperature: °C Incubation time:
	Short term storage at: °C Interval of transfer:

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the Laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte

Nukleinsauren" (5. uberarbeitete Fassung BMFT)

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Thermational depository action (s).

Number, symbols etc., given to the microorganism by the depositor.

It is stronty recommended that the taxonomic desinguation and/or scientific description (see under VII.) of the

microorganism be indicated.

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/fungi (first page) 0488

III. COMDITIONS FOR LONG TERM STORAGE	(X) ⁵
IV. CONDITIONS FOR TESTING VIABILITY	(x) ⁵
V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(x) ⁵
Description of components:	
Method(s) for checking presence of components:	
i !	
] 	
1	

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH OR ENVIRONMENT'
Mazard group of the microorganisms named under I. according to DIN 58 956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9:
THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL 1:
() L1
() 13
IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ? () YES (X) NO
(if yes, please specify:) (X) ⁵
(X) the undersigned is not aware of such properties
IF THE MICROORGANISM IS GENETICALLY MANIPULATED:
1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:
general genetic recombination (rec):
sensitivities:
resistances:
modifications:
restrictions:
auxotrophies:
2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:
3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).
1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY MAVE NO PATHOGENIC POTENTIAL.
() YES
2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.
() YES
IN THE LATTER CASE PLEASE NOTE:
According to the regulations of the ZKBS ⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS ⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form 1. The DSM only accepts for deposit micrographisms which belong to hazard group I or II, according to DIM

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukomoinierte Nukleinsauren" (5. uberarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

ZKBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

II. SCIE	NTIFIC DESCRIPTION	× x) ⁵
		()8
II. ADO	ITIONAL DATA	()
		i
		•
. DEPOS	ITOR ⁹	
		Land James Kil
		The state of the s
me:	Biogen, Inc.	Signature:
		James F. Haley, Jr.
		Ivor R. Elrifi
		Attorneys for Biogen, I Fish & Neave
dress:	14 Cambridge Center	Date: 875 Third Avenue
	Cambridge, Massachusetts 02142	New York, New York 10D
	02142	
		19/3/
		1-7-27

of the microorganism be indicated.

Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).

The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are

required. Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

RECOGNITION OF THE DEPOSIT OF MICROOR ISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

. IDENTIFICATION OF THE MICROORGANISM	
dentification reference given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY.
HFIF-F	DOM 1053
M5219 (G-pPLa-HFIF-67-12Δ19)	DSM 1853
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIG	NATION
The microorganism identified under I. above was accompanied by:	
() a scientific description (X) a proposed taxonomic designation	
(Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganis on 1981-10-01 (Date of original deposit) ¹	m identified under I. above, which was received by it
IV RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this I (date of original deposit) and a request to convert the original depreceived by it on 1991-10-24 (date of receipt of request)	osit to a deposit under the budapest Treat, was
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name. DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN Gm	or of authorised official(s):
Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Date 1991-10-28

Where Ruls 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired Form DSM-BP/4 (sole page) 0291

COGNITION OF THE DEPOSIT OF MICROORGA'
FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

VIABILITY STATEMENT issued pursuant to Rule 10.2 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM		
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1853 Date of the deposit or of the transfer 1: 1981-10-01		
III. VIABI	LITY STATEMENT	•		
On that d: (ity of the microorganism identified under II above was testeste, the said microorganism was X)3 viable 3 no longer viable SITIONS UNDER WHICH THE VIABILITY TEST HAS B			
IV. INTE	RNATIONAL DEPOSITARY AUTHORITY			
Name:	DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Mascheroder Weg 1 B D-3300 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorised official(s): Date: 1991-10-28		

Indicate the date of original deposition, where a new deposition a transfer has been made, the most recent relevant date (date of the new deposition date of the transfer).

Form DSM-BP/9 (sole page) 0787

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

³ Mark with a cross the applicable box.

⁴ Fill in if the information has been requested and if the results of the test were negative.

German Collection of Mic. Jiganisms

GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH

DSM - Grisebachstrasse 8 - D-3400 Gottingen, Germany

Tel. (05 51) 39 38 22 / 39 38 23

ACKNOWLEDGEMENT OF RECEIPT AND ACCEPTANCE

The microorganism mentioned below has been deposited with the Deutsche Sammlung von Mikroorganismen.

Name and address of depositor:

BIOGEN N.V. 24 Handelskad Willemsted.

Curacao, Netherland Antilles

Identification reference of the microorganism used by the depositor:

HFIF-G M5219 (G-pPlc-HFIF-67-8)

Taxonomic designation of the microorganism provided by the depositor:

Escherichia coli

DSN accession number of the microorganism:

DSN 1854

Date of receipt of the viable microorganism:

June 5, 1980

In addition to the identification reference and the taxonomic designation the depositorXHAS proximal / has not provided a scientific description of the microorganism.

igotimes The microorganism has been sent to the DSM directly by the depositor.

The microorganism has been sent to the DSM on benalf of the depositor by the following depository under the designation and accession number given:

As stated by the depositor the microoganism may be rendered accessible to any third party under the following conditions:

O without any restrictions

 \otimes according to Rule 28 EPC and to the agreement between the European Patent Organisation and the DSN (Official Journal EPO 5, 301-307, 1978) and/or

according to the Swedish patent legislation and to the agreement between the Swedish Patent Office and the DSM (Swemsk Patenttidning nr 12, 1979)

in accordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form P 2570)

in accordance with a) Title 37, Code of Federal Regulations, section 1.14 (37.CFR 1.14) and Title 35, United States Code, section 122 (35 U.S.C. 122) of the United States of America and b) without any restriction on availability to the public of the culture upon granting of a United States patent wherein the deposited microorganism is part

of the disclosure of the invention

in accordance with the French patent law

in accordance with the conditions as specified by the depositor on enclosed separate sheet.

Göttingen, June 5,1980

Place

date

DEUTSCHE SAMMLUNG VON MIKROORGANISMEN Signature

achait für Biotechnologiache Forschung mbH Grisebachstraße &

D-3400 Göttingen

Gesellschaft für Biotechnologische Forschung mbH. Mascheroder Weg 1, 3300 Braunschweig, Tel.: (05.31) 70.08—1, Telex: 9—5.26.87

Vorsitzender des Aufsichtsrats Min. Dir. Dr. Friedrich Bischoff

Geschäftstührer: Dr. Maria-Regina Kula Dr. Helmut Zeitträger

Gebr. Lobbooke, Braunschweig Konto 23 781 (8LZ 270 305 00) Registergericht: Amisgericht Drawnsch HRB 477

(German Collection of Microorgani)

ACCESSION FORM for

deposition of patent microorganisms

DSM accession number:

Date culture received:

DSM 1354

5 June 11.

The microorganism mentioned below is to be deposited with the DSH on account of a patent application (to be) filed with The deposit is made in secondance with Rule 28 EPC / with the Swedish patent legislation (delete, if not applicable) Name and address of depositor: BIOGEN N.V. 24 Handelskad Willemsted Curacao, Netherland Autilles Identification reference of the HFIF - G microorganism given by the depositor (strain number, symbols etc.): M5219 (G- pPLc - HFIF - 67-8) Taxonomic designation of the E. coli microorganism: A scientific description of the microorganism is attached on a sengrate sheet: YES 🗌 The microorganism to be deposited in a pure culture a mixture of strains : YES [In case of a mixed culture, please give a concise description on a separate sheet-about the components and methods to determine their viability. Does the microorganism and/or iat metabolic products present any harard for man, animals, plants or the environment: (if any, please specify on a separate sheet): YES [NO 🔯 Ine microorganism will be ment to the DSH directly by the depositor. The microorganism will be sent to the DSM on behalf of the depositor by the following depository under the designation and accession number given: The microorganism may be rendered accessible after receipt and deposition to any third party without any restriction according to Rule 28 EPC and to the agreement between the European Pstent Organization and the DSM (Official Journal EPO $\underline{5}$, 301-307, 1978) and/or according to the Swedish patent legislation and to the agreement between the Swedish Pstent Office and the DSM (Svensk Patenttioning nr 12, 1979) in scrordance with the "Declaration of Release" to be filed by the depositor with the DSM and the German Patent Office (at present Form 2750) in accordance with a) Title 37, Code of Federal Regulations, Section 1.14 (37.CFR 1.14) and Title 35, United States Code aection 122 (35 U.S.C. 122) of the United States of America and b) without any reatrictions on the availability to the public of the culture

in accordance with the conditions at specified by the depositor on enclosed separate sheet.

(Please mark what applies)

upon granting of the United States patent wherein the deposited microorganism is parts.

in accordance with the French patent law

FISH & NEAVE

875 THIRD AVENUE

A PETER ADLEM

TICLARDA PAL

LIBAE, CRISTAL

DAVIDA. LOG WENNYE.
JOHN J. CAMBINO NAM
LINBAA WADLER
KELSEY I. DIX
MARTA E. GRODB
JOHN M. RITORELLA
WILLIAM J. MCCARE
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VICEI B. VECNIEN
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ANISTINE MACKETT BERANDA BERLAS-MICHAEL P MORRIS MICHAEL
HICHAELP HODRIS
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JERENY LACK
EVAN M GBELL
JANESP BERGIN
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JEFFET M RESPN
LIAMNA C RALMAM
BRADFORD L FRIEDMA
DESTAA BURGELIA
MORETTAA BURGELIA
MORETTAA BURGELIA

CHARLES SHITH
DAVIDW DLANT
ALBERTE FET
WERRESTS SCHWART
LARS I RULLESEID
WILLIAM J. BLERETH
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MANES F MALEY, JR MICHARD M BARNES LAURENCE B ROGERS THOMAS L, BLANKEYTI VIOLENT W BALLADING MODERT J. GOLDMAN THOMAS L. BECREST DAMES W. BARTY DAMES W. BARTY

NEW YORK. N.Y. 10022-6250 TELEPHONE. (212) 715-0600 TELEX: 14-8367 CABLE ADDRESS: PISHNEAVE TELECOPIER: IZIZI 715-0674

October 16, 1991

1885-1830 CHABLES HEAVE 1867-1937

> Deutsche Sammlung von Mikroorganismen Und Zellkulturen GmbH Mascheroder Weg 1b D-3300 Braunschweig Federal Republic of Germany

> > Biogen - B8/B8 CIP Deposits DSM 1791-1793; 1851-1854

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Please note that the original depositor has undergone a corporate name and address change from Biogen N.V., 24 Handelskad, Willemsted, Curacao, Netherland Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hesitate to contact us.

Thanks for your help.

Yours very truly,

*Jel James F. Haley,

Ivor R. Elrifi

Attorneys for Biogen, Inc.

JFH/IRE:bb Enclosures

BLDAPEST TREATY ON THE INTERNATIONAL

RECOGNITION OF THE DEPOSIT OF MICROORGANISMS

FOR THE PURPOSE OF PATENT PROCEDURE

STATEMENT IN THE CASE OF AN ORIGINAL DEPOSIT pursuant to Rule 6.1

DEUTSCHE SAMPLLING VON MIKROORGANISMEN UND ZELLKULTUREN GODH Mascheroder Weg 1b 0-3300 Brounschueig Federal Republic of Germany

To	be	fil	led	in	by th	e Des	06 i ti	ary A	uthor	ity	
	054	-Aç	zes:	sian	numb	er:					
	Dat	e c	ulti	re i	rece i	ved :					

BACTERIA/FUNGI

THE UNDERSIGNED HEREBY DEPOSITS UNDER THE BUDAPEST TREATY THE MICROGREANISM IDENTIFIED HEREUNDER AND UNDERTAKES NOT TO WITHDRAW THE DEPOSIT FOR THE PERIOD SPECIFIED IN BULE 9.12

I. IDENTIFICATION OF THE MICROORGANISM		
Identification reference ³ : HFIF-G M5219 (G-pPLc-HFIF-67-8) Taxonomic designation ⁴ : Escherichia coli	The culture to be deposited is: (X) a pure culture () a mixture of microorganisms (Mark with a cross where applicable)	
11. COMDITIONS FOR CULTIVATION	(x) ⁵	
as according to original deposit application DSM 1854	pH before sterilisation: Sterilisation min at *C pH after sterilisation: Oxygen relationship: () aerobic () micromerophilic () obligate anaerobic Specific gaseous requirements:	
	Incubation temperature: °C Incubation time: Short term storage at: °C Interval of transfer:	

This form may also be used if the undersigned converts into a deposit under the Budapest Treaty the deposit of a microorganism that he or his predecessor in title has already deposited, outside the Budapest Treaty, with the same depositary institution either before (Rule 6.4(d)) or after the acquisition by that institution of the status of international depositary authority.

Number, symbols etc., given to the microorganism by the depositor.

It is stronly recommended that the taxonomic desingnation and/or scientific description (see under VII.) of the

microorganism be indicated.

Mark with a cross if additional information is given on an attached sheet.

Form DSM-BP/1-Bacteria/Fungi (first page) 0488

¹ The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIM 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren' (5. uberarbeitete Fassung BMFT)

TOPAGE	(x) ⁵
III. COMDITIONS FOR LONG TERM STORAGE	
	(X) ⁵
IV. CONDITIONS FOR TESTING VIABILITY	
	İ
V. COMPONENTS OF MIXED CULTURES (WHEN APPLICABLE)	(X) ⁵
V. CUMPUNERIS UP HIACU COLLONES (CHES APPLICATION	
Description of components:	
Mezer throat at positions.	
Method(s) for checking presence of components:	
T. Control of the Con	

⁵ Mark with a cross if additional information is given on an attached sheet.

VI. PROPERTIES DANGEROUS TO HEALTH OR ENVIRONMENT
Nazard group of the microorganisms named under I, according to DIN 58 956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9:
THE STRAIN HAS TO BE HANDLED UNDER THE FOLLOWING LABORATORY CONTAINMENT LEVEL 1:
() L1 () L2
() 13
IS THIS STRAIN DANGEROUS TO HEALTH OR THE ENVIRONMENT ? () YES (X) NO
(if yes, please specify:)
(X) the undersigned is not aware of such properties
IF THE MICROORGANISM IS GENETICALLY MANIPULATED:
1. PLEASE INDICATE ALL THE RELEVANT GENETIC PROPERTIES:
general genetic recombination (rec):
sensitivities:
resistances:
modifications:
restrictions:
auxotrophies:
2. DESIGNATION OF THE DONOR ORGANISM(S), THE DNA OF WHICH HAS BEEN CLONED INTO THE PLASMID:
3. If the strain is genetically manipulated the depositor must take appropriate steps to prove any pathogenic potential (see: ZKBS guidelines or equivalent national guidelines.) Please specify whether (WITHOUT A DEFINITE ANSWER TO THESE QUESTIONS THE ORGANISM CANNOT BE ACCEPTED FOR DEPOSITION).
1. THE SUBGENOMIC FRAGMENTS OF THE DNA DEFINETLY MAVE NO PATHOGENIC POTENTIAL.
() YES
2. THE SUBGENOMIC FRAGMENTS HAVE A PATHOGENIC POTENTIAL.
() YES
IN THE LATTER CASE PLEASE NOTE:
According to the regulations of the ZKBS ⁶ the DSM can only accept genetically manipulated, potentially pathogenic organisms for deposition when a copy of the permit issued by the ZKBS ⁶ (or by an equivalent national biological safety commission) for work on the organisms accompanies the deposition form

The DSM only accepts for deposit microorganisms which belong to hazard group I or II, according to DIN 58956 (Beiblatt 1) Teil 1, Medizinische Mikrobiologie, ISBN 3-410-12028-9 and can be handled under the laboratory containment level L1 or L2 according to "Richtlinien zum Schutz vor Gefahren durch in-vitro neukombinierte Nukleinsauren" (5. uberarbeitete Fassung BMFT)

Mark with a cross if additional information is given on an attached sheet.

2KBS = Zentrale Kommission für Biologische Sicherheit (Central Commission for Biological safety)

	NTIFIC DESCRIPTION	(x) ⁵
/III. ADOI	ITIONAL DATA	()8
X. DEPOSI	TOR ⁹	J Liles VI
ame:	Biogen, Inc.	Signature: Fifth Staff
		James F. Haley, Jr! Ivor R. Elrifi Attorneys for Piogen, Inc
ddress:	14 Cambridge Center Cambridge, Massachusetts 02142	Date: Fish & Neave 875 Third Avenue New York, New York 1002
		10/19/12

It is strongly recommended that the scientific description and/or proposed taxonomic designation (see I.) of the microorganism be indicated.

8 Mark with a cross if additional information (other than the information referred to in footnote 4 is given on an attached sheet, such as the source of the microorganism, the name(s) and the address(es) of any other depositary institution(s) with which the microorganism has been deposited, or the criterion used when drafting the proposed taxonomic designation (The supplying of such information is optional).

9 The name of the depositor must be identical with the signature.

The name of the depositor must be identical with the signature.

In case of a legal entity the signatures of two representatives, officially nominated by this entity, are required.

Where the signature is required on behalf of a legal entity, the typewritten name(s) of the natural person(s) signing on behalf of the legal entity should accompany the signature(s).

RECOGNITION OF THE DEPOSIT OF MICROOR ISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM	
Identification reference given by the DEPOSITOR	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY
HFIF-G	
M5219 (G-pPlc-HFIF-67-8)	DSM 1854
II. SCIENTIFIC DESCRIPTION AND/OR TAXONOMIC DESIGNAT	ION
The microorganism identified under I. above was accompanied by: () a scientific description (X) a proposed taxonomic designation	
(Mark with a cross where applicable)	
III. RECEIPT AND ACCEPTANCE	
This International Depositary Authority accepts this microorganism ide on 1981-10-01 (Date of original deposit) ¹	entified under I. above, which was received by it
IV RECEIPT OF REQUEST FOR CONVERSION	
The microorganism identified under I above was received by this Intern (date of original deposit) and a request to convert the original deposit received by it on 1991–10–24 (date of receipt of request for	to a deposit under the Duapeter
V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name. DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):
Adress: Mascheroder Weg 1 B D-3300 Braunschweig	Date: 1991-10-28

Form DSM-BP/4 (sole page) 0291

Where Rule 6.4(d) applies, such date is the date on which the status of international depositary authority was acquired

COGNITION OF THE DEPOSIT OF MICROORG/ 4S
FOR THE PURPOSES OF PATENT PROCEDURL

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

VIABILITY STATEMENT issued pursuant to Rule 10.2 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. DEPOSITOR		II. IDENTIFICATION OF THE MICROORGANISM	
Name: Address:	Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY DSM 1854 Date of the deposit or of the transfer ¹ : 1981-10-01	
III. VIABI	LITY STATEMENT		
On that da	ity of the microorganism identified under II above was teste ate, the said microorganism was X) ³ viable 3 no longer viable ITIONS UNDER WHICH THE VIABILITY TEST HAS B		
IV. INTE	RNATIONAL DEPOSITARY AUTHORITY		
Name:	DSM DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s):	

Indicate the date of original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date if the new deposit or date of the transfer).

3 Mark with a cross the applicable box.

Form DSM-BP/9 (sole page) 0787

² In the cases referred to in Rule 10.2(a) (ii) and (iii), refer to the most recent viability test.

⁴ Fill in if the information has been requested and if the results of the test were negative.



DSM - Mascheroder Weg 1b - D-38124 Braunschweig

Fish & Neave Attn. Ivor R. Elrifi 1251 Avenue of the Americas New York, NY 10020 USA

Ihr Zeichen / Your ref.

Unser Zeichen / Our ref.

Tel.

Datum / Date

05 31 / 26 16 -

P 110 94/H

254

28.04.1994

Deposit DSM 1854 - Eschericia coli HFIF-G M5219 (G-pPLc-HFIF-67-8)

Dear Sirs,

we herewith confirm that the strain

Escherichia coli HFIF-G M5219 (G-pPLc-HFIF-67-8)

has been deposited at the DSM under the number DSM 1854 bearing the above mentioned identification reference. By a typographical error made in DSM the capital <u>L</u> in the designation G-pPLc-HFIF-67-8 has been misprinted as a small 1. This is not correct. We regret this typographical mistake and send to you the newly filled in statements of receipt and acceptance in English and German stating the correct identification reference.

Yours faithfully,

DSM-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH

U. Weils

Dr. Vera Weihs

RECEIVED

MAY - 2 1994

TED BY

FISH & NEAVE - PATENT DEPT.

-

Note: The old incorrect forms may be destroyed.

BUDAPESTER VERTRAG ÜBER DIE INTERNATIONALE ANERKENNUNG DER HINTERLEGUNG VON MIKROORGANISMEN FÜR DIE ZWECKE VON PATENTVERFAHREN

INTERNATIONALES FORMBLATT

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

EMPFANGSBESTÄTIGUNG BEI ERSTHINTERLEGUNG, ausgestellt gemäß Regel 7.1 von der unten angegebenen INTERNATIONALEN HINTERLEGUNGSSTELLE

I. KENNZEICHNUNG DES MIKROORGANISMUS						
Vom HINTERLEGER zugeteiltes Bezugszeichen: HFIF-G M5219 (G-pPLc-HFIF-67-8)	Von der INTERNATIONALEN HINTERLEGUNGSSTELLE sugeteilte EINGANGSNUMMER: DSM 1854					
II. WISSENSCHAFTLICHE BESCHREIBUNG UND/ODER VORG	ESCHLAGENE TAXONOMISCHE BEZEICHNUNG					
Mit dem unter I. bezeichneten Mikroorganismus wurde						
() eine wissenschaftliche Beschreibung (X) eine vorgeschlagene taxonomische Bezeichnung						
eingereicht. (Zutreffendes ankreuzen).						
III. EINGANG UND ANNAHME						
Diese internationale Hinterlegungsstelle nimmt den unter I bezeichneten Mikroorganismus an, der bei ihr am 1981–10–01 (Datum der Ersthinterlegung) ¹ eingegangen ist.						
IV. EINGANG DES ANTRAGS AUF UMWANDLUNG						
Der unter I bezeichnete Mikroorganismus ist bei dieser Internationalen Hinterlegungsstelle am 1980-06-05 eingegangen (Datum der Ersthinterlegung) und ein Antrag auf Umwandlung dieser Ersthinterlegung in eine Hinterlegung gemäß Budapester Vertrag ist am 1991-10-24 eingegangen (Datum des Eingangs des Antrags auf Umwandlung).						
V. INTERNATIONALE HINTERLEGUNGSSTELLE						
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN Gmbl Anschrift: Mascheroder Weg 1b D-38124 Braunschweig	Unterschrift(en) der zur Vertretung der internationalen Hinterlegungsstelle befugten Person(en) oder des (der) von ihr ermächtigten Bediensteten: Color Color Datum: 1994-04-28					
	Datum: 1994-04-28					

¹ Falls Regel 6.4 Buchstabe d sutrifft, ist dies der Zeitpunkt, su dem der Status einer internationalen Hinterlegungsstelle erworben worden ist.
Formblatt DSM-BP/4 (einsige Seite) 12/93

BUDAPEST TREATY ON THE INTERNAT. AL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

Biogen Inc. 14, Cambridge Center Cambridge Massachusetts USA 02142

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page

I. IDENTIFICATION OF THE MICROORGANISM		
Identification reference given by the DEPOSITOR: HFIF-G M5219 (G-pPLc-HFIF-67-8)	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: DSM 1854	
II. SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXONOMIC DESIGNATION		
The microorganism identified under I. above was accompanied by:		
() a scientific description		
(X) a proposed taxonomic designation		
(Mark with a cross where applicable).		
III. RECEIPT AND ACCEPTANCE		
This International Depositary Authority accepts the microorganism identified under I. above, which was received by it on 1981-10-01 (Date of the original deposit) ¹ .		
IV. RECEIPT OF REQUEST FOR CONVERSION		
The microorganism identified under I above was received by this International Depositary Authority on 1980-06-05 (date of original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on 1991-10-24 (date of receipt of request for conversion).		
V. INTERNATIONAL DEPOSITARY AUTHORITY		
Name: DSM-DEUTSCHE SAMMLUNG VON MIKROORGANISMEN UND ZELLKULTUREN GmbH Address: Mascheroder Weg 1b D-38124 Braunschweig	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorized official(s): Date: 1994-04-28	

Form DSM-BP/4 (sole page) 12/93

Where Rule 6.4 (d) applies, such date is the date on which the status of international depositary authority was acquired.



BOARD OF TRUSTEES REPRESENTING - American Assecution of Immunoissists e American Institute er Bieregical Sciences · American Phytosatheropical Seciety e American Seciety of Biological Chemists e American Society for Microbiology American Security of Parasitologists

· American Society of Zoelogists

HEAR SOCIETY OF Tradical Medicine and mygone ARRES SACIONY OF AMERICA * Intections Oncomes Secrety of America

· Mycological Society of America

Phational Bossach Council-Mational Academy of Sciences - Secrety of Protezooregitts

• 301-881-26CC

TYPE CULTURE COLLECTION AMERICAN

12301 PARKLAWN DRIVE ROCKVILLE, MARYLAND 20852

February 27, 1981

. Trame Culture Association

James F. Haley, Jr., Esq. Attorney for Biogen N.Y. c/o Fish & Neave 277 Park Avenue New York, New York 10172

Gentlemen:

We received on February 26, 1981 a deposit of cultures of organisms identified as Escherichia coli M5219(G-pPLa-HFIF-67-12AMI), HFIF-H, and Escherichia coli HB101(p 125)-qHFIF-4), HFIF-I.

These strains have been assigned the ATCC numbers 31824 and 31825, respectively.

We understand that these organisms are being deposited in the American Type Culture Collection (ATCC) in connection with the filing of an application for a patent.

We further understand that the deposit of these cultures does not grant to ATCC during the effective term of the patent anticipated a license, either expressed or implied to infringe the patent, and our release of these cultures to others does not grant them a license, either expressed or implied, to infringe the patent.

We further understand that if these cultures should die or be destroyed during the effective life of the patent it shall be your responsibility to replace them with living cultures of the same organisms.

We agree in consideration for a one-time service charge, not to distribute these cultures or any information relating thereto or to their deposits until such time as a parent has been issued disclosing the above deposits except in accordance with a U.S. Parent Office Rule of Practice, Rule 14, or until you authorize us to make these strains available. After a patent is issued and we are so informed the cultures will be made available for distribution to the public. The ATCC agrees to maintain the cultures for a period of 30 years from the deposit date. Non-payment of the service charge within 90 days of the deposit date relieves the ATCC from the above provisions.

Payment in the amount of \$1,140.00 received. Thank you.

Sincerely yours,

Dolelie A. Praulan By: (Mrs.) Bobbie A. Brandon

An independent non-profit organization incorporated in Washington, D. C. and devoted to the preservation of reference cultures and their distribution to the scientific community

A RICAN TYPE CULTURE COVECTION

12301 Parklawn Drive . Rockville, Maryland 20852 . 301 861 2600

Data sheet to be completed by depositors to the 3/824 COLLECTION OF BACTERIA

	Scientific name of organism F. ml; ME219 (C-pDTa-UFTF-57-12AMT) Do not urite in this box 3/22:1-
1.	
2.	train designations other than ATCC number
٦.	Is this the type strain of this organism (see reverse side)?
١.	Is this the type strain of this organism (see that the type If this strain has been designated in the literature as the type strain, please cite reference:
- 5- ,	Base and address of depositor: Biogen N.V. 15 Pietermaai Curacao, Netherlands Antilles
_	Isolated by
٥.	isolated by date
	I FUE
7.	If you did not isolate this strain, indicate from whom you received if:
	ATCC - depositor -
8.	Reason for deposit: Requested by ATCC
	Requested by ATCL Rev taxon: Species Subepecies Assay of
	Produces the antibieticPatent
	Production ofOther
9.	Maintenance: Medium (attach formula) LB Broth or bactotryptone Medium (attach formula) LB Broth or bactotryptone
	28°C LB Broth supplemented with 25 A.S.
	a) Does this organism survive: Freeze drying? Yes Freezing? Yes (poully) b) Recommended method for long-term preservation: b) Recommended method for LDR Proth/Glycerol or DMSO at -80°C
•	Is this strain roopsthogenic? NO If so, would you classify it as class 2, 3, or at (see reverse side for description of classes)
12.	Is this strain phytopathogenic: NO (Information required by Flant Quarantine Division, USDA) If so, a) Is the geographical distribution of this organism general, limited, or unanown (encircle): b) Vould you recommend that this strain be made available to any qualified investigator regardless of his location: c) If not, what limits would you place on the distribution of this strain?
	. Please attach a complete description of this strain unless description is given in accompanying reprint.
14.	. References (Please enclose two (2) of each pertinent reprint, if available):
15	
	Do not heat above 28°C.
	Signature of Depositor
AĪ	CC Form 1-3 (1971) Attorney for Biogen N.V.

AN AICAN TYPE CULTURE COL CTION

12301 Parklayn Drive . Rockville, Maryland 20852 . 301 881 2600

Data sneet to be completed by depositors to the

	Scientific name of organism E.coli HB101(D[325]-dHF1F-4) Do Not only the Mile See
1.	Scientific hade of organization HFIF-I Arcc / 3/825
2.	Strain designations other than Alta hands
,	Accession cate
٠.	If this strain has been designated in the literature as the type Date received 2/26/8/
L .	if this strain has been designated in the little attack.
5.	Name and address of depositor: Biogen N.V. 15 Pietermaai
	Curacao, Netherlands Antilles
6.	Isolated by
	from date
	If you did not isolate this strain, indicate from whom you received it:
7.	If you did not isolate this strain, or
	ATCC - depositor -
Α.	Reason for deposit:
••	Requested by ATCE
	Produces the antibiotic Assay of
	Production of Other Patent
. 9 .	Maintenance: Medium (attach formula) LB Broth or bactotryptone
•	Hedium (attach formula) LB Bloth of Sabbook and a sich 100 ag/ml carbonic
	Temperature Other LB Broth supplemented with 100 Ag/ml carbenic
	TemperatureOther DB Block State Compared to the compa
10.	and a second company protery protection:
	Freeze drying or LB Broth/glycerol or DMSO at 300 C
11.	In this strain compathogenic? NO If so, would you classify it as class 2, 3, or 4? (see reverse side for description of classes)
	No. (a. a.
12.	Is this strain phytopathogenic: NO (Information required by Flant Quarantine Division, USDA) If so, a) Is the geographical distribution of this organism general, limited, or unknown (encircle); b) Vould you recommend that this strain be made available to any qualified
	to the target of the location:
	c) If not, what limits would you place on the distribution of this strain?
13.	Please attach a complete description of this strain unless description is given in accompanying reprint.
1 k .	References (Pleass enclose two (2) of each pertinent reprint, if available):
•-•	
15.	Conments:
	$\bigcirc \qquad \bigcirc \qquad$
•	Je J. Holly te
	Signature of Lapositury
AT	CC Form 1-8 (1971) Attorney for Biogen N.V.

FISH & NEA1 :

875 THIRD AVENUE

NEW YORK, N.Y. 10022-6250

TELEPHONE IZIZI 715-0600 TELEX 14-8367

CABLE ADDRESS FISHNEAVE TELECOPIER (212) 715-0674

October 16, 1991

CHARLESS SHITDAVID J.ES
DAVID J ---(855-1930 CHARLES HEAVE 1867-1937

> Mrs. Bobbie Brandon American Type Culture Collection 12301 Parklawn Drive Rockville, MD 20852

Down weed Time constant Time const JOHN F MARD EDWARD J DEFRANCD NAME D ROWLAND POILIPPE V RIESEN MARE D ENGELNANN MARS D ENGLISHME ERIC & MURBARD DAVID A LDEWENSTEIN LINDRA WADLER RELECT NIZ NASTA E BROSS JOHN N NINTI JOHN B STORLLA CHRISTONNERS GODDIETY
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A PETERADLES RICHARDA IRZ

----ABISTIMA MACETTADO AMERICA JUDIDAME DE GRADO A DEBLAS MICHAEL E MODRES JUDIDAME DE GRADO ATRANCE MACETADA MACET

Biogen - B8/B8 CIP Deposits identified as ATCC 31824 and ATCC 31825

Dear Mrs. Brandon:

JANES F NALET. JR BICHARDN BARNES

AND THE PROPERTY OF THE PROPER

VINCENT W PALLADING MOBERT J GOLDMAN THOMAS L. BECREST DANIEL W GANTY WOMMAN W BEAMER REVIN'J CULLIGAN GLENIA O WETENGOUT BUSAN BROGOFF WARGARETA PIERO

SELLBELM INDERMYN DONGTWY GITBE MA DONE SHAFWY MUMBET TOWNS

We have enclosed two (2) requests for conversion of the above-identified deposits to meet the requirements of the Budapest Treaty. The ATCC designations, as well as the strain designations given by the depositor, are identified on the request forms. In addition, we enclose copies of the letter of receipt of these deposits and of the original deposit applications containing the media and culture requirements.

Please note that the original depositor has undergone a corporate name and address change, from Biogen N.V., 15 Pietermaai, Curacao, Netherlands Antilles, to Biogen, Inc., 14 Cambridge Center, Cambridge, Massachusetts, U.S.A. 02142. This name and address change has been duly registered according to the national laws in the Patent Office of each country where a patent application has been filed referencing these deposits.

If you have any questions or require further information, please do not hestiate to contact us.

Thanks for your help.

Yours very truly,

James F. Haley,

Ivor R. Elrifi

Attorneys for Biogen, Inc.

JFH/IRE:bb Enclosures

12301 Parkiawa Drive · Rockville, MD 20852 USA · Telephone: (301)881-2600 Telex: 898-055 ATCC NORTH

TO DEPOSIT OR TO CONVERT A DEPOSIT TO MEET THE REQUIREMENTS OF BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

1.	Name of deposit (microorganism, cell, seed, plasmid, etc.) (G-pPLA-HFIF-67-12 \Delta MI)	
2.	Strain designation given by the depositor (number, symbols, etc.) HFIF-H	
	Is this an original deposit under the Budapest Treaty?	
١.	Is this a request for a conversion of a deposit already at the ATCC to meet the requirements of the Budapest Treaty? (If so, indicate ATCC designation.) Yes, ATCC 31824	
i.	Is this deposit a mixture of microorganisms or cells?	
Details and conditions necessary for the cultivation of the strain, for its storage and for testing its via also, where a mixture of microorganisms is deposited, descriptions of the components of the mixture an one of the methods permitting the checking of their presence.		
	see attached sheets	
	An indication of the properties of the strain which are or may be dangerous to health or the environment, or an indication that the depositor is not aware of such properties. Depositor is not aware of any properties of the strain which are or may be dangerous to health or	
	properties of the strain which are of may be dangerous to hearth of	
	environment.	
	a. For cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics (if so list the antibiotics)	
	b. For hybridoma deposits please complete. What is the isotype of antibody produced?	
	Is this strain zoopathogenic? No phytopathogenic?	
	Does this strain contain plasmids relevant to the patent process? If so, what physical containment level is required for experiments as described in the National Institutes of Health Guidelines involving Recombinant DNA Molecules (i.e., PI, P2, P3 and P4 facility)? P1	
þ	answers to these questions are recommended but not required.	
	FOR ATCC USE ONLY	
	ATCC DESIGNATION	
	DATE CULTURE RECEIVED	
	DATE VIABILITY TEST COMPLETED	



12341 Parklawn Drive . Rockville, MD 20852 USA . Telephone: (361)881-2600 Telex: 898-055 ATCC NORTH

TO DEPOSIT OR TO CONVERT A DEPOSIT TO MEET THE REQUIREMENTS OF BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

	Escherichia coli		
1. 1	Name of deposit (microorganism, cell, seed, plasmid, etc.) HB101 (p[325]-qHF1F-4)		
	Strain designation given by the depositor (number, symbols, etc.)		
	s this an original deposit under the badapes.		
1	s this a request for a conversion of a deposit already at the ATCC to meet the requirements of the Budapest Freaty? (If so, indicate ATCC designation.) Yes, ATCC 31825		
. 1	s this deposit a mixture of microorganisms or cells?		
2	Details and conditions necessary for the cultivation of the strain, for its storage and for testing its viability and also, where a mixture of microorganisms is deposited, descriptions of the components of the mixture and at least one of the methods permitting the checking of their presence. See attached sheets		
- . /	An indication of the properties of the strain which are or may be dangerous to health or the environment, or an indication that the depositor is not aware of such properties. Depositor is not aware of any		
	properties of the strain which are or may be dangerous to health or		
-	the environment.		
	a. For cell culture deposits please complete. Is the cell being cultured in the presence of antibiotics (if so list the antibiotics)		
	b. For hybridoma deposits please complete. What is the isotype of antibody produced?		
. 1	s this strain zoopathogenic? NO phytopathogenic? No		
. 1	Ooes this strain contain plasmids relevant to the patent process? If so, what physical containment level is required for experiments as described in the National Institutes of Health Guidelines involving Recombinant DNA Molecules (i.e., P1, P2, P3 and P4 facility)? P1		
Ъе	answers to these questions are recommended but not required.		
	FOR ATCC USE ONLY		
	ATCC DESIGNATION		
	DATE CULTURE RECEIVED		
	DATE VIABILITY TEST COMPLETED		



n Drive · Rockville, MD' 20052 USA · Telephone: (301)231-5520 Telex. «48-655 ATCCNORTH · FA »: 301-770-2587

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2
To: (Name and Address of Depositor or Attorney)

James F. Haley, Jr., Ivor R. Elrifi Fish & Neave 875 Third Avenue New York, NY 10022

Identification Reference by Depositor:

Deposited on Behalf of: Biogen, Inc. (Docket B8/B8 C 1P)

Escherichia coli M5219 (G-pPLA-HFIF-67-12deltaMI), HFIF-H
Escherichia coli HB101 (p[325]-qHFIF-4), HFIF-I
31824

The deposits were accompanied by: ____ a scientific description X a proposed taxonomic description indicated above.

The deposits were received <u>February 26, 1981</u> by this International Depository Authority and have been accepted. A request to convert the deposits to a deposit under the Budapest Treaty was received on October 23, 1991.

AT YOUR REQUEST:

X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years after the date of deposit, and for a period of at least five years after the most recent request for a sample. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested October 25, 1991. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA.

Signature of person having authority to represent ATCC:

Bobbie A. Brandon, Head, ATCC Patent Depository

Date: October 28, 1991

ATCC Designation

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International Depository Authority: American Type Culture Collection, Rockville, Md. 20852 USA

Signature of person having authority to represent ATCC:

mand

Date: May 6, 1994

Bobbie A. Brandon, Head, ATCC Patent Depository